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ENCEPHALITIS WITH INTRANUCLEAR INCLUSION BODIES

A CLINICOPATHOLOGIC STUDY

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The presence of type A intranuclear inclusion bodies in the central nervous system of patients dying of encephalitis is a rare phenomenon. Dawson [1] has reported 2 such cases. In a review of the literature in which so-called inclusion bodies have been described he found no previous reports in which the inclusions were clearly distinguished from products of cellular degeneration. He concluded that no distinctive cellular changes characteristic of virus disease have previously been reported in cases of human encephalitis.

Recently, Smith, Lennette and Reames [2] reported the only case of fatal encephalitis, that of an infant, in which intranuclear inclusion bodies were present and a virus identical with that of herpes simplex was isolated from the brain. Sabin and Wright [3] described a case of fatal virus infection in a laboratory worker in whom transverse myelitis

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1. Dawson, J. R., Jr.: (*a*) Cellular Inclusions in Cerebral Lesions of Lethargic Encephalitis, Am. J. Path. **9**:7, 1933; (*b*) Cellular Inclusions in Cerebral Lesions of Epidemic Encephalitis: Second Report, Arch. Neurol. & Psychiat. **31**:685 (April) 1934.

2. Smith, M. G.; Lennette, E. H., and Reames, H. R.: Isolation of the Virus of Herpes Simplex and the Demonstration of Intranuclear Inclusions in a Case of Acute Encephalitis, Am. J. Path. **17**:55, 1941.

3. Sabin, A. B., and Wright, A. M.: Acute Ascending Myelitis Following a Monkey Bite, with the Isolation of a Virus Capable of Reproducing the Disease, J. Exper. Med. **59**:115, 1934.

and visceral necrosis developed after the bite of a monkey. Sabin[4] isolated a B virus in this case which showed a generic relationship to the viruses of pseudorabies and herpes simplex.

In the study of his 2 cases Dawson[1] was unable to transmit the disease to mice, guinea pigs, monkeys, rabbits, dogs or chickens. Since herpes virus is known to produce fatal encephalitis in rabbits, he concluded that the virus concerned was not that of herpes. Moreover, the nuclear inclusions observed by Dawson were not of the very large granular type associated with herpes infection. The inability to transmit the disease to monkeys also suggests that the agent was not the B virus of Sabin.

The purpose of this report is to present the clinical and pathoanatomic observations in a case of fatal human encephalitis which bore a resemblance clinically and pathologically to the cases reported by Dawson. In this case type A intranuclear inclusion bodies were abundant in nerve cells and neuroglia and the topographic distribution of the lesions differed to a pronounced degree from that seen in those diseases of the nervous system which are commonly regarded as being of a virus nature.

REPORT OF A CASE

W. L., a white boy aged 5 years, was admitted to the Strong Memorial Hospital on Oct. 25 and died on Dec. 15, 1940.

Present Illness.—The patient had been in good health until twelve days before admission, when he awoke during the night crying and frightened but finally returned to sleep. The next morning the parents noticed stiffness and twitching of the left arm, which was held in a flexed position. This gradually increased, and five days later twitching and rigidity of the left leg appeared. These twitchings progressed to such extreme dystonic movements that the patient would fall backward on standing. The dystonia ceased during sleep. Throughout the ensuing week these involuntary movements became more severe, but the patient was well oriented, ate and slept well, was apparently afebrile and had no headaches nor vomiting. Transient urinary retention developed five days before admission.

History.—The family history was not remarkable. The birth and early development were normal. There was no history of infectious disease. No history of a similar disease was found by the family physician, Dr. Charles T. Adams, in the community or among the domesticated stock. At the age of 15 months (1937) mastoidectomy on the left side was performed and recovery was uneventful. In July 1940, three months before admission, the patient ran a nail into his right foot, and the wound was incompletely healed at the time of admission. Tetanus antitoxin was not administered prior to admission to the hospital.

Physical Status.—The temperature was 38 C. (100.4 F.), the pulse rate 130 and the respiratory rate 18 a minute. The patient was well developed and well

4. Sabin, A. B.: Studies on the B Virus: I. The Immunological Identity of a Virus Isolated from a Human Case of Ascending Myelitis Associated with Visceral Necrosis, Brit. J. Exper. Path. **15**:248, 1934; II. Properties of the Virus and Pathogenesis of the Experimental Disease in Rabbits, ibid. **15**:268, 1934; III. The Experimental Disease in Macacus Rhesus Monkeys, ibid. **15**:321, 1934.

nourished. He appeared semistuporous but responded slowly, answering questions in a dysarthric manner, and was well oriented and cooperative. An almost completely healed puncture wound was found on the sole of the right foot, and there was an infected scratch wound on the dorsum of the left hand. The tonsils were large, and the nasopharynx was slightly injected. Examination of the chest revealed nothing abnormal.

Neurologic Status.—The outstanding feature was the irregular occurrence (every one to five minutes) of hyperkinetic seizures on the left side, best designated as rapid torsion spasms. In these dystonic seizures, in which the muscles of the left spinal group appeared to predominate, the back, but not the neck, was arched and the trunk was flexed to the left. In the interval between seizures the left leg remained spastic and in extension and the left arm was spastic, adducted and flexed at the elbow, with the hand tightly clenched and sharply flexed at the wrist against the precordium. With the onset of the seizure this posture would become greatly accentuated, with resultant pseudo-opisthotonos and turning of the body in an arc to the left. The head and eyes were not involved in this dystonia. The dystonic seizures disappeared during sleep, but the posture between the seizures remained unchanged. The motor system of the right side was not remarkable. The deep reflexes were hyperactive but equal on the two sides, and no clonus could be elicited. The Babinski response was not obtained, and the Kernig and Brudzinski signs were absent. Sensory examination was unsatisfactory, but the patient responded to painful stimulation adequately over both sides. The cranial nerves were normal.

Studies of the Spinal Fluid

Date, 1940	Initial Pressure, Mm.	Protein, Mg. per 100 Cc.	Sugar, Mg. per 100 Cc.	Chlorides, Mg. per 100 Cc.	Colloidal Gold Curve	Mononuclear Cells per Cu. Mm.	Pandy Reaction	Wassermann Reaction
10/25	200	25	80	700	5554431000	3	1+	—
10/31	Low	30	75	679	5552211000	3	1+	—
11/ 2	Low	20	100	...	.....	5	1+	—
11/ 3	200	20	...	...	.....	3	1+	..
11/ 5	100	30	100	...	.....	3	—	..
11/10	80	35	73	...	.....	5	—	..
11/30	160,	25	86	755	1110000000	2	—	—
12/12	Low	110	..	...	.....	5	1+	..

Laboratory Studies.—Urine: Urinalysis on admission and subsequently gave normal results.

Blood: On admission there were 4,650,000 red cells per cubic millimeter and 15 Gm. of hemoglobin per hundred cubic centimeters. The white cell count was 13,350, with 87 per cent polymorphonuclears, 7 per cent lymphocytes and 6 per cent monocytes. Subsequent studies of the blood on November 2 revealed 11,000 white cells, with 59 per cent polymorphonuclears and 41 per cent lymphocytes; on November 5, 25,000 white cells; on November 9, 5,180,000 red cells, 16.0 Gm. of hemoglobin and 20,500 white cells, with 65 per cent polymorphonuclears and 35 per cent lymphocytes, and on November 15, 12,300 white cells. Blood cultures were sterile on several occasions. The Wassermann and Kahn reactions of the blood were negative, as were the results of agglutination tests with Brucella abortus. Calcium of the blood measured 10.8 mg., phosphorus 3.8 mg., phosphatase 5.2 units and nonprotein nitrogen 28 mg. per hundred cubic centimeters. The icterus index was 4, and a trace of lead was found on spectroscopic examination.

Stools: Studies on admission revealed nothing remarkable.

Cultures: Cultures of material from the nose and throat were repeatedly negative for Corynebacterium diphtheriae and pneumococci. On several occasions

Staphylococcus aureus was present. Cultures of material from the lesion on the dorsum of the left hand yielded a beta hemolytic streptococcus and no anaerobes.

Spinal Fluid: Cultures were repeatedly negative. Other findings are presented in the table.

Electroencephalograms (November 11 and 16, Dr. John B. Hursh): Large (100 to 150 microvolts), slow (2 to 4 per second) pathologic waves occurred over the entire scalp.

Course in Hospital.—The fluctuations of the body temperature are shown in figure 1. No somatic cause for the hyperthermia could be demonstrated by clinical or laboratory procedures.

The course was progressively downhill. The dystonic seizures became more frequent and severe. On November 1 slight spasticity and occasional jerking movements were observed in the right side, and during the second week (November 2 to 9) the dystonic seizures involved both sides of the body, so that opisthotonos-like states occurred (fig. 2). Occasional tremors of the tongue and extremities appeared. Dysphagia developed, along with transient ocular palsies, dysphonia and weakness of the lower left side of the face. On November 10 an extensor response on plantar stimulation was found on the right side. Transient decreases in the severity of the dystonic seizures occurred during the third week, probably as a result of the continued use of chloral hydrate.

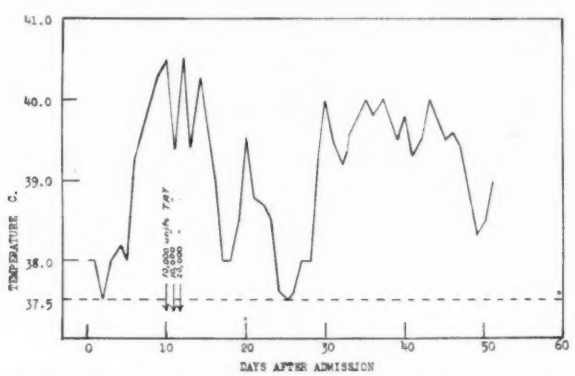

Fig. 1.—Temperature chart. *TAT* indicates tetanus antitoxin.

During the next three weeks (November 16 to December 7) urinary incontinence and frequent fecal impaction developed. He became more and more comatose and took fluids poorly. Daily changes in the neurologic picture occurred, including the development of sensory hypesthesias, conjugate deviation of the eyes to the right, retraction of the head with rotation to the right, transient changes in the deep reflexes and the Babinski response and occasional states of hypotonia. During the last week of life the spasticity of the extremities decreased considerably and the opisthotonos-like seizures became infrequent. The patient died December 15, nine weeks after the onset of symptoms.

Acetylsalicylic acid and quinine proved inefficacious during the hyperthermia. Because of the possibility of chronic tetanus the patient was given a total of 40,000 units of tetanus antitoxin shortly after admission (fig. 1). Large doses of vitamin B complex, thiamine hydrochloride and vitamin E were employed. Treatment was otherwise symptomatic and sedative.

Pathoanatomic Studies.—The autopsy was performed sixteen hours after death. Apart from changes in the nervous system, gross and microscopic examination revealed marked emaciation and muscular atrophy. A large thrombus was present in the right external iliac vein, and several emboli were observed in the large and small pulmonary vessels, which were probably the immediate cause of death. Acute tracheobronchitis and patchy bronchopneumonia were present.

Macroscopic Examination of the Central Nervous System: The brain weighed 1,280 Gm. The dura mater was not remarkable, and the leptomeninges were smooth, thin and glistening. The blood vessels over the entire cerebrum were markedly engorged. The brain appeared swollen and soft. Large areas of softening could be felt over the lateral and inferior surfaces of the right frontal lobe. After fixation in dilute solution of formaldehyde U. S. P. (1:10), sections of the brain revealed discrete and diffuse areas of softening, with discoloration and marked vascular congestion throughout the cortex of both hemispheres. In several regions, notably the lateral and orbital surfaces of the frontal lobe and the insula of the right hemisphere, the softening had progressed to frank diffuse necrosis, with the formation of irregular cystlike spaces containing friable debris (fig. 3 *A* and *B*). Smaller discrete areas of necrosis were present in the left occipital cortex (fig. 3 *C*). Such lesions involved partially or completely the

Fig. 2 (Nov. 16, 1940).—*A*, position of body in the intervals between opisthotonos-like seizures. *B*, position of body at the height of the seizure.

entire depth of the cortex but usually stopped short of the white matter. Apart from the cortical lesions, marked discoloration of the right lenticular and thalamic nuclei suggested early necrosis (fig. 3 *B*). The brain stem, the cerebellum and the spinal cord appeared essentially normal.

Microscopic Examination of the Nervous System: The leptomeninges appeared slightly edematous and showed surprisingly little reaction histologically. In those regions where the underlying cortex was most severely involved the leptomeninges showed only slight infiltration with occasional lymphocytes, plasma cells and *Gitterzellen*. The blood vessels were generally heavily engorged with erythrocytes.

No portion of the cerebral cortex was free from pathoanatomic change. The cortex showed remarkably diffuse involvement, affecting nerve cells, glia elements and blood vessels in a ubiquitous manner (fig. 4 *A*, *B* and *C*). The blood vessels were engorged with erythrocytes (fig. 5 *A*). No thromboses or hemorrhages were found. In the areas of most severe necroses the endothelial cells of the intima of the blood vessels were slightly swollen, and moderate perivascular infiltrations with lymphocytes and plasma cells were present (fig. 4 *B* and *C*). Occasional infiltrations with hematogenous mononuclear cells were found about the congested

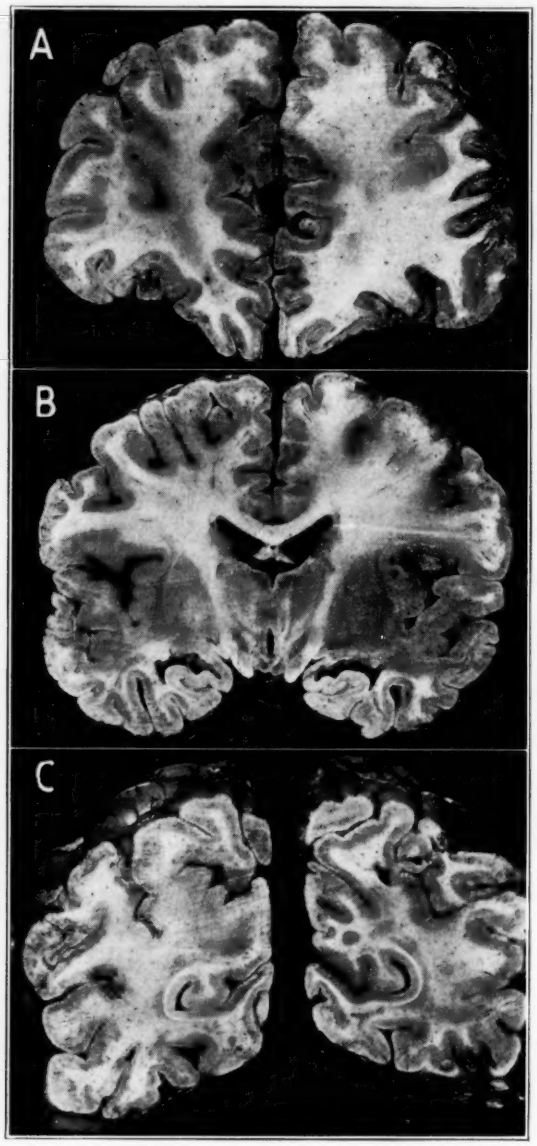

Fig. 3.—*A*, transverse section through the frontal lobes to show the maximal degree of necrosis over the lateral and inferior surfaces of the right frontal lobe. The left frontal lobe is involved to a lesser degree. × 0.5.

B, transverse section through the corpora mamillaria. The entire cortex is congested, and necrosis prevails in the frontal lobe and the Island of Reil on the right side. The lenticular nuclei and thalami are deeply pigmented and show early necrosis on the right side. × 0.4.

C, transverse section through the occipital lobes to show congestion of blood vessels and discrete areas of necrosis in the cortex on the left. × 0.5.

Fig. 4.—*A*, photomicrograph from area FG of von Economo of the right frontal lobe, showing complete necrosis of the cortex, the moderately infiltrated perivascular spaces and the relative absence of leptomeningeal involvement. Hematoxylin-eosin stain; × 30.

B, photomicrograph from area FG of von Economo of the left frontal lobe, showing the moderate infiltration of the perivascular spaces, the numerous rod cells and the striking loss of nerve cells in the cortex. The leptomeninges are relatively free of involvement. Thionine stain; × 100.

C, higher magnification of a portion of the field shown in *B*. The nerve cells show liquefaction of cytoplasm, and the nuclei are vacuolated, with margination of the basichromatin at the nuclear membrane. The nucleolus, when present, is pushed out against the nuclear membrane. Neuronophagia by microglia and neuroglia cells is present to a slight degree. Most of the microglia cells have been transformed into rod cells. The endothelial cells of one blood vessel (*X*) appear swollen. Thionine stain; × 430.

vessels in the underlying white matter, and a few lymphocytes and plasma cells were seen free in the cortex. Occasional mitotic figures were observed in these mononuclear cells "lying free in the parenchyma." This suggests that lymphocytes and plasma cells can multiply within areas of inflammation in the central nervous system.

The typical lesion was an acute necrosis of the nerve cells and, to a less degree, of the neuroglia. The early stages of this process were most evident in the parietotemporal region of both sides and over the right occipital and the left frontal lobe. This was marked by swelling of the nucleus and cytoplasm, often accompanied by dispersion of the Nissl granules into small peripheral clumps (suggestive of Nissl's acute and profound changes in the nerve cells). In the nuclei of such cells, both in hematoxylin-eosin and in Giemsa sections, small, occasionally multiple, refractile, homogeneous and eosinophilic inclusion bodies could be distinguished (fig. 5 *B*). Associated with the presence of these bodies there were usually partial solution and peripheral margination of the chromatin particles of the nucleus, resulting in a clear, halo-like space surrounding the inclusions and a distinct thickening of the nuclear border. The nucleolus could be clearly distinguished in such cells, often as a dark mass closely attached to the heavy nuclear border. Further changes were characterized by an eccentric position of the entire nucleus and profound changes in the cytoplasm. In many cells the cytoplasm assumed a distinct eosinophilic stain and became shrunken and condensed. In other cases the cells appeared to be undergoing autolysis, the margins becoming ragged and indistinct. In these cells small, irregular vacuoles were seen in the cytoplasm, giving a pale and foamy appearance. Large, irregular perineural spaces were prominent about such cells. In these severely involved nerve cells the intranuclear inclusion bodies were greatly enlarged and filled the nucleus completely as a dark, homogeneous and eosinophilic mass (fig. 5 *B*). Ultimately these cells disintegrated completely. The latter changes, leading to complete necrosis, were most evident in the right frontal and the left occipital lobe. True neuronophagia was rarely seen; the best example of such a phenomenon was found in the dentate nucleus of the cerebellum, where the process was relatively mild (fig. 5 *C*).

The neuroglia in the cortex and in the subcortex underlying the necrotic cortex was ubiquitously involved in the destructive process. In those areas of moderate or early involvement (parietotemporal lobes) the microglia cells were frequently transformed into rod cells, the astrocytes showed hypertrophy with swelling of cytoplasm and an occasional oligodendroglia cell disclosed small intranuclear inclusion bodies. In the areas of necrosis, such as the right frontal lobe, the microglia cells were completely transformed into *Gitterzellen,* the astrocytes showed regressive alterations (clasmatodendrosis) and large intranuclear inclusion bodies were seen frequently in the oligodendroglia cells of the cortex and in the adjacent white matter. Intranuclear inclusion bodies were never found in the microglia cells, and very rarely in the astrocytes.

In those regions where the process was moderately severe small sharply outlined masses of material were seen in the cytoplasm of occasional nerve cells and glia cells. With the hematoxylin-eosin stain they were nonrefractile. Such masses were usually much smaller than the nucleolus. Similar cytoplasmic inclusions have been interpreted by various authors[5] as products of cellular disinte-

5. Da Fano, C.: The Histo-Pathology of Epidemic (Lethargic) Encephalitis, Brit. M. J. **1**:153, 1921. Meleney, H. E.: Degeneration Granules in Brain Cells in Epidemic Encephalitis, Arch. Neurol. & Psychiat. **5**:146 (Feb.) 1921.

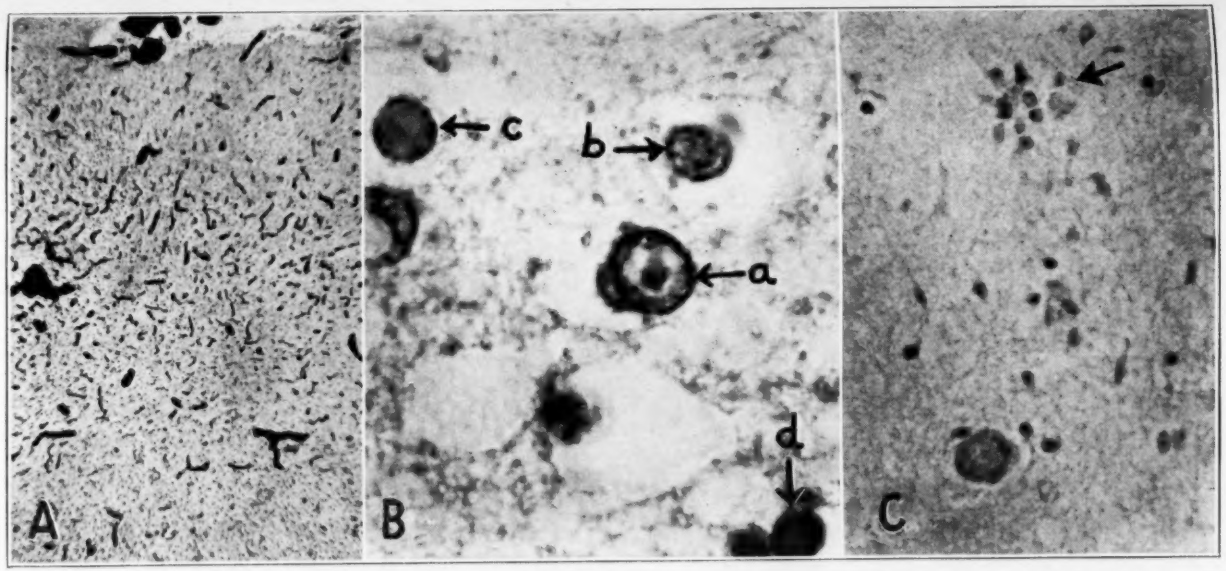

Fig. 5.—*A*, photomicrograph from area FD of von Economo of the left frontal lobe, illustrating the excessive congestion of the blood vessels in the cortex and leptomeninges in a region in which the nerve cells have been almost completely destroyed but actual necrosis has not occurred. Note the complete absence of myelinated fibers. Smith-Quigley myelin stain; × 30.

B, photomicrograph from area FC of von Economo of the right frontal lobe, illustrating the various types of intranuclear inclusion bodies. At *a* is a small, centrally placed body with an unstained halo surrounding it. At *b* is a larger body. The inclusion body at *c* completely fills the nucleus. The nuclear material is severely disorganized, and the basichromatin has collected on the nuclear membrane. The cytoplasm of the nerve cells has become completely liquefied. At *d* is a small inclusion body in the nucleus of an oligodendroglia cell. Giemsa stain; × 1,500.

C, photomicrograph from the left dentate nucleus, showing complete neuronophagocytosis of a nerve cell. Thionine stain; × 430.

gration. No cytoplasmic inclusions similar to those described in the nucleus were seen.

Myelin stains revealed variable changes. In the areas of slight involvement the fibers in the zonal and supraradiary layers were diminished in number, while the radiary layer appeared uninvolved. In the subcortex no areas of demyelination were found, even in those areas where occasional oligodendroglia cells with intranuclear inclusion bodies were seen. These observations, incidentally, tend to refute Levaditi's [6] hypothesis that demyelination may be due to an oligodendrocytotropic virus. In areas, such as the right frontal lobe, where necrosis was marked myelin had disappeared entirely from the cortex and subadjacent medullary

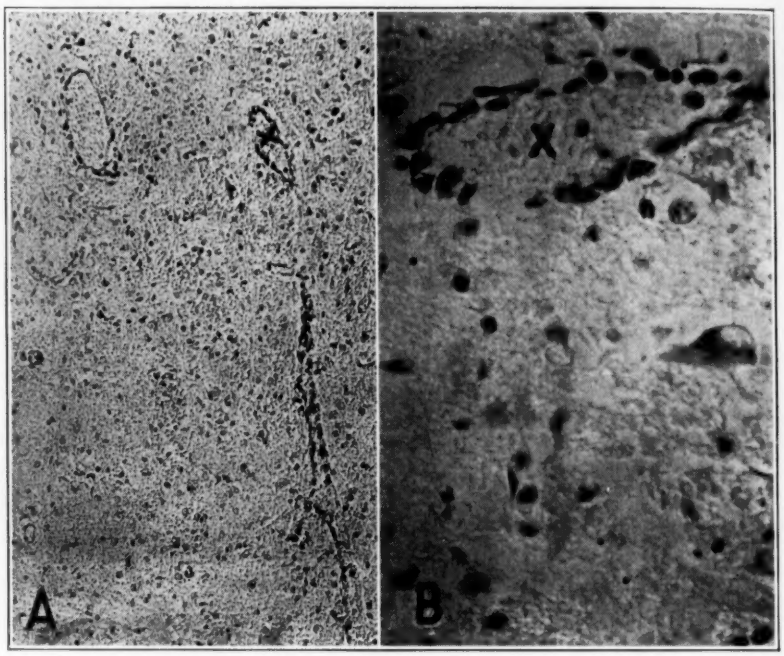

Fig. 6.—*A*, photomicrograph from the head of the right caudate nucleus, showing the moderate perivascular infiltration and almost complete absence of nerve cells. Thionine stain; × 100.

B, higher magnification of a portion of the field shown in *A*. The mere shadows of former nerve cells can be seen, and hematogenous cells (lymphocytes and plasma cells) are found in the perivascular spaces and lying free in the parenchyma. This area represents an early stage of parenchymatous necrosis. The blood vessel marked *X* is the same as that in *A*. Thionine stain; × 430.

layer. The neurofibrillae showed variable changes, being related in degree to the severity of damage in the myelinated fibers and parenchyma.

6. Levaditi, C.: Les ultravirus provocateurs des ectodermoses neurotropes, Ann. Inst. Pasteur **45**:673, 1930.

Over the right frontal pole (area FE of von Economo) typical coagulation necrosis was observed. This was the only area in which this type of change was present.

Apart from the cerebral cortex, the deep nuclear masses showed variable degrees of involvement. The caudate nucleus, the putamen, the globus pallidus and the claustrum on the right showed histologic changes characteristic of early necrosis. On the left side early changes similar to those seen in the parietotemporal cortex were present and consisted essentially of the presence of intranuclear inclusion bodies in nerve cells and oligodendrocytes, hypertrophied microglia cells, pulverization of Nissl granules and a variable amount of perivascular infiltration with mononuclear cells (fig. 6 *A* and *B*). The thalami were involved to a moderate degree. The anterior portion of the hypothalamus showed slight histopathologic changes. The posterior portion of the hypothalamus, the corpora Luysi, the red nuclei, and the substantia nigra on both sides were, at most, involved to a minimal degree. The hindbrain showed no changes other than vascular congestion, with occasional perivascular infiltration with mononuclear cells. In the cerebellum, the Purkinje and granular cells were well preserved, and except for an occasional cell which was undergoing neuronophagia the dentate nuclei were intact (fig. 5 *C*). The spinal cord and the cranial and peripheral nerves showed no histopathologic changes.

COMMENT

Clinical Aspects.—The clinical course in our case is similar to that in Dawson's second case.[1b] Both patients were young, and the onset of the disease was sudden and not preceded by prodromal symptoms.

In all 3 cases sudden dyskinetic movements occurred, although in our case the movements were unilateral at the beginning. The dyskinesia disappeared during sleep; however, the extreme spasticity in the left extremities remained unchanged. The temperature was at first normal, or only slightly elevated, but later rose and remained high until death. In contrast to the course in Dawson's first case [1a] but identical with that in his second case, there was no remission after the illness set in. The course of the illness was progressively downhill, the duration being two months in our case, as compared with four months in Dawson's second case.[1b] In our case the involvement of the central nervous system became increasingly widespread, resulting in bilateral signs early in the illness and accompanied by bulbar signs toward the end.

In contrast to the progress of the disease in these cases is the more rapid course in the case of herpes encephalitis reported by Smith, Lennette and Reames [2] and in the case of virus B infection described by Sabin and Wright.[3] The pronounced meningeal signs and the more rapid course in Japanese (type B), St. Louis and equine encephalomyelitis also differentiate the clinical pictures in these diseases. There are, however, certain similarities to the hyperkinetic form of the type A epidemic encephalitis of von Economo. As Muckenfuss [7] has emphasized,

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7. Muckenfuss, R. S.: Epidemic Encephalitis, Bull. New York Acad. Med. **17**:487, 1941.

it is impossible to differentiate the various forms of epidemic encephalitis on clinical grounds alone. Similarly, it is impossible to differentiate clinically this type of encephalitis from the other forms whch are commonly accepted to be of a virus nature.

The changes in the spinal fluid in the present case are of interest. Similar to the observations in Dawson's second case, the cell count was normal, and the pressure was normal or only slightly increased. The sugar content was slightly elevated, and the chlorides were normal. The total protein content was normal, ranging from 25 to 35 mg. per hundred cubic centimeters until three days before death, when it rose to 110 mg. The latter change may be explained by a possible rupture of necrotic cortical material through the pial-glial membrane into the subarachnoid space. Lange's colloidal gold curve was of paretic type early in the disease but became normal shortly before death. According to Foster and Cockrill [8] and Greenfield and Carmichael,[9] reduction in the first zone of Lange's gold curve is occasionally found in the von Economo (type A) form of epidemic encephalitis. Consequently, changes in the spinal fluid give no clue to the diagnosis of this condition.

The presence in the electroencephalogram of large delta waves over the entire scalp suggests a diffuse destructive process and is nonspecific.

Clinicoanatomic Correlations.—In view of the diffuse character of the process it is, of course, hazardous to attempt to correlate the clinical signs with the lesions present in the central nervous system, but certain interesting features may be worthy of comment. The lesions in the right lenticular complex may have resulted in the dyskinetic movements which ushered in the clinical picture. The greater severity of the process in the right frontal lobe suggests that this region may have been the primary site of involvement and that this occurrence may be related to the early predominance of spasticity on the left side. The later appearance of spasticity on the right is perhaps a result of the early pathoanatomic changes in the left frontal lobe. It is interesting to note the terminal diminution of spasticity and the early involvement of the motor cortex, with severe damage to the Betz cells, especially in the right hemisphere. This interpretation is contradictory to the experimental observations of Fulton [10] and Fulton and Kennard.[11] The prominent bulbar signs at the

8. Foster, H. E., and Cockrill, J. R.: Cerebrospinal Fluid in Encephalitis Lethargica, Am. J. M. Sc. **167**:696, 1924.

9. Greenfield, J. G., and Carmichael, E. A.: The Cerebro-Spinal Fluid in Clinical Diagnosis, New York, The Macmillan Company, 1925, p. 170.

10. Fulton, J. F.: Spasticity and the Frontal Lobes: A Review, New England J. Med. **217**:1017, 1937.

11. Fulton, J. F., and Kennard, M. A.: A Study of Flaccid and Spastic Paralyses Produced by Lesions of the Cerebral Cortex in Primates, A. Research Nerv. & Ment. Dis., Proc. (1932) **13**:158, 1934.

end of the illness find no correlation with the postmortem observations in the hindbrain.

The bouts of pyrexia, refractory to management by drugs and unassociated with clinical or postmortem evidence of somatic origin, are probably best explained as a result of involvement of the central nervous system. Nerve cells in the hypothalamus showed only slight injury, but both thalami showed a moderate degree of histopathologic change. It is not possible, however, to exclude the general systemic effect, at least late in the disease, of the widespread necrosis of brain substance, and the terminal picture was complicated by the terminal bronchopneumonia.

Pathoanatomic Aspects.—It is unfortunate that the autopsy did not include an attempt to isolate the virus. Three pathoanatomic observations, however, are of aid in differentiating the disease in this case from the various forms of encephalitis of proved or suspected virus origin. The most important morphologic distinction is the presence of type A intranuclear inclusion bodies in the nerve cells and to a less degree in the oligodendrocytes. Such bodies have not been found in the von Economo (type A), the Japanese (type B), the St. Louis or the Russian form of epidemic encephalitis, in the western or the eastern form of equine encephalitis or in poliomyelitis. According to Cowdry,[12] intranuclear inclusion bodies can be divided into two groups: type A, as seen in the Lipschütz bodies of herpes febrilis and herpes zoster and the elementary bodies found in cases of varicella, virus B infection and yellow fever, and type B, as seen in the Nicolau bodies of herpes febrilis and herpes zoster and the inclusion bodies of poliomyelitis, Rift Valley fever and equine encephalomyelitis. In the type B group there is usually only slight reaction in the nucleus, margination of basichromatin is absent and the reaction in the surrounding tissue is not marked. In the type A group, however, the nuclear material is severely damaged, the basichromatin collects on the nuclear membrane and the surrounding tissue shows a severe reaction. It is evident that the eosinophilic intranuclear bodies in our case and in the 2 cases reported by Dawson [1] belong to the type A group of Cowdry's classification. The inclusion bodies found in cases of herpes are large and granular, whereas in our case the large inclusions are distinctly homogeneous. Dr. Marguerite G. Smith, who has studied the bodies in this case, states they are quite distinct morphologically from those in the case in which she isolated the herpes simplex virus.[2] Dr. James R. Dawson, who has also studied the inclusion bodies in our case, finds that they are somewhat larger than those present in his 2 cases, but is inclined to discount this difference.

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12. Cowdry, E. V.: The Problem of Intranuclear Inclusions in Virus Diseases, Arch. Path. **18**:527 (Oct.) 1934.

The topographic distribution of the lesions in Dawson's cases and in our case is rather unique and is quite different from that found in the commonly recognized virus diseases of the nervous system. In our case there were severe involvement of the cerebral cortex, moderate involvement of the lenticular nuclei and thalami, slight minimal changes in the midbrain, hindbrain and cerebellum and absence of pathoanatomic changes in the spinal cord. Dawson found a similar, but probably more general, distribution in his cases.

Gross necrosis of parenchyma was not found by Dawson in either of his cases, while it was a prominent feature in our case. Necrosis is common in cases of the Japanese (type B) and the St. Louis form of epidemic encephalitis and was present in the cases of Smith and associates [2] and Sabin and Wright,[3] but considerations previously mentioned seem to differentiate the disease in the present case from the conditions in these cases. It is possible that the infecting agent in our case was more virulent than in the cases of Dawson and may account for the extreme necrosis.

Two incidental observations should be emphasized. The occurrence of mitotic figures in lymphocytes and plasma cells lying free in the parenchyma suggests the possibility that these cells can multiply within areas of inflammation in the central nervous system. The presence of intranuclear inclusion bodies in oligodendroglia cells in the medullary layer of the brain in which no loss of myelin occurred does not confirm Levaditi's hypothesis [6] that the demyelination in various myelinoclastic diseases is due to an oligodendrocytotropic virus.

SUMMARY AND CONCLUSIONS

A clinicopathologic study of a necrotic form of encephalitis with type A intranuclear inclusion bodies is reported. The topographic distribution of the lesions is unlike that found in those diseases of the nervous system which are commonly regarded as being of a virus nature.

From a review of the literature it is probable that this is a form of encephalitis described originally by Dawson.

VARIATIONS IN ELECTROENCEPHALOGRAM ASSOCIATED WITH ELECTRIC SHOCK THERAPY OF PATIENTS WITH MENTAL DISORDERS

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In the course of administering electric convulsion therapy to a group of psychotic and psychoneurotic patients at the New York State Psychiatric Institute and Hospital, a series of electroencephalographic observations were made in order to determine what changes the electroencephalogram might undergo as a result of such treatment.

In the application of electric shock therapy one of two main types of response ordinarily may be obtained: (1) a minor attack, resembling a petit mal epileptic attack, or (2) a generalized convulsive seizure.[1] The minor response consists essentially, immediately on passage of the electric current through the brain, of a state of unconsciousness or unawareness of the surroundings for a variable period, usually from one to sixty seconds, associated with apnea. Infrequently, simultaneous with the passage of the current, there is an initial generalized jerk of the body. After the period of unconsciousness, or the "petit mal" seizure in the strict sense of its meaning,[2] the next phase is ushered in, consisting of a variable period of confusion and disorientation, which gradually diminishes in severity and intensity. This period of confusion is usually not maintained longer than two minutes, although rarely it may continue longer. After this the patient regains full consciousness but exhibits characteristically an amnesia, partially retrograde, for the treatment. He subsequently may remember events occurring only until the time of application of the electrodes to the temples, but has no

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1. Kalinowsky, L., and Barrera, S. E.: Electric Convulsion Therapy in Mental Disorders, Psychiatric Quart. **14**:719, 1940.

2. Kalinowsky, L.; Barrera, S. E., and Horwitz, W. A.: "Petit Mal" Response in Electric Shock Treatment and Its Relationship to Epilepsy, read at the American Psychiatric Association, Richmond, Va., May 9, 1941.

memory for the events immediately following this until return of consciousness. A variable period of apnea occurs immediately after the administration of the electric current and usually lasts for from ten to thirty seconds, rarely exceeding fifty seconds. The generalized convulsion resulting from the passage of the electric current through the brain resembles a grand mal epileptic paroxysm and is not grossly dissimilar to the metrazol convulsion, so far at least as the tonic and final clonic phases are concerned. There does not appear to be the so-called primary clonic phase which has been described for the metrazol seizure.[3] Frequently, after passage of the "shocking" current there is a latent period of from one to thirty seconds preceding the onset of the convulsion, during which the patient is apneic, quiet and unconscious. Very often the period of apnea is prolonged for a number of seconds after the termination of the seizure, and then stertorous breathing ensues. In general, the period of confusion following the electrically induced convulsion does not seem to be quite so long as that which has been observed after metrazol-induced convulsions. The patient usually regains consciousness in about five minutes after the convulsive shock and recovers from his marked confusional state in from ten to twenty minutes. As was mentioned with respect to the minor attack, retrograde amnesia is also observed in all patients subjected to the convulsions.

The total number of electric shocks administered to the patients and the number of major and minor attacks induced varied from case to case. Each patient, however, received a total of from 1 to 22 electric shock applications, the usual number varying from 8 to 16 shocks. The frequency with which treatments were given remained constant, three times a week.

MATERIAL AND METHODS

A two channel, ink-writing electroencephalograph, constructed by Mr. Walter E. Rahm Jr., was used to obtain recordings of brain potentials. In each case six electrodes were firmly placed on the scalp by means of collodion, contact between the electrodes and the scalp being made by means of electrode jelly placed in a small depression in each electrode. The sites used on the scalp included the prefrontal, motor and occipital regions on corresponding areas of each side of the midline, as illustrated somewhat roughly in the diagram (fig. 1). The bipolar method of recording potential variations was utilized. In this way, brain wave patterns could be obtained by using fronto-occipital (*FO*) leads (right and left), motor occipital (*MO*) leads (right and

3. Strauss, H.; Landis, C., and Hunt, W. A.: The Metrazol Seizure and Its Significance for the Pathophysiology of Epileptic Attack, J. Nerv. & Ment. Dis. **90**:439, 1939.

left), frontomotor (*FM*) leads (right and left) and transfrontal, transmotor and transoccipital (*TF*, *TM* and *TO*) leads.

A total of over 350 electroencephalograms were obtained on a group of 61 patients receiving electric shock therapy at the New York State Psychiatric Institute and Hospital. The observations may be divided into two main groups: (1) those associated with individual shocks resulting in (*a*) minor, or "petit mal," seizures or (*b*) major, or generalized, convulsive seizures, and (2) those associated with administration of successive shocks and with the effects remaining after cessation of the course of therapy.

Electroencephalograms were obtained immediately after 20 separate "petit mal" attacks and 15 grand mal convulsions, a total of 35 records. In all instances of minor attacks, readings were taken continuously until the brain potentials attained, or at least approximated, their preshock

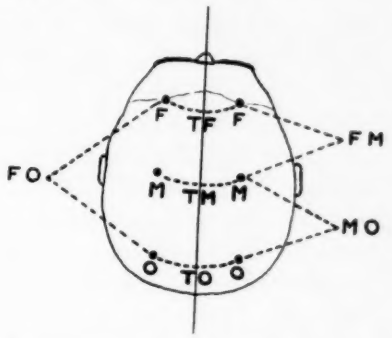

Fig. 1.—Points of application of the electrodes on the scalp are noted. The vertex and indifferent electrodes were not included in this diagram. However, the vertex electrode is placed nearly midway from left to right between the motor electrodes.

appearance and had maintained this appearance for at least five minutes. In several of the cases in which generalized convulsions were exhibited recordings were continuous until the normal, or preshock, pattern predominated for at least twenty minutes, while in a number of the other cases, after about twenty minutes to one-half hour of continuous recordings, subsequent readings were taken at short intervals during the day until the predominating wave patterns resembled the normal, or preshock, electroencephalograms and had maintained this pattern for at least twenty minutes. Electroencephalograms were also obtained on the different patients at various intervals during the course of treatment and subsequent to termination of treatment, so as to evaluate the effects of successive electric shock treatments on the electroencephalogram in terms of temporary effects and possible permanent changes.

In 4 instances electroencephalographic recordings were made during the actual passage of the current through the brain, but this practice was discontinued because of the possible dangerous consequences entailed in electrically grounding the patient. Furthermore, the passage of a large current through the amplifying and recording systems always resulted in a temporary "block" of these systems and thereby produced only a straight or slightly wavy line on the recording tape for about ten to twenty seconds.

A number of readings were taken during the actual convulsive movements, but these records were practically valueless for purposes of interpretation, since the violent muscular movements produced irregular high voltage, high frequency wave patterns which masked, for the most part, the actual brain potentials.

RESULTS

I. CHANGES ASSOCIATED WITH INDIVIDUAL SHOCKS

A. *"Petit Mal" Response (Minor Seizure).*—A "petit mal" attack was associated in every instance with definite electroencephalographic changes, which, however, were somewhat variable from one person to another but were generally constant for any one subject. For purposes of presentation we may divide the record into three phases. During the first phase, which corresponds clinically to the period of apnea and total unconsciousness, there is marked "irregularity" in the electroencephalographic pattern, with waves of mixed frequency, varying from 3 to 40 cycles per second. Regular trains of alpha activity do not appear. In some cases the electroencephalographic pattern during this period shows mainly high voltage, 4 to 6 cycle per second waves with waves of higher frequency superimposed on or interposed between them. Most frequently, however, low voltage activity, consisting of 8 to 30 cycle per second waves of irregular and bizarre forms, is scattered at random through these records. In addition, 4 to 7 cycle per second waves of moderate voltage appear. The type of the pattern obtained in each instance is apparently dependent in some degree on the type of the record noted immediately preceding the administration of the shocking current and also on the relative severity of the "petit mal" response. Apparently, the more severe the clinical response, the greater will be the incidence of slow potentials, although this does not hold in all instances. Furthermore, the greater the amplitude and incidence of alpha activity prior to shock, the more frequent the appearance of slow, high voltage waves. The pattern noted during the first clinical phase (apnea and complete unconsciousness) persists for about twenty to twenty-five seconds after passage of the shocking current. The second phase of the record now appears, corresponding clinically to the latter part of the period of unconsciousness and to the period of confusion and disorienta-

tion. Here the amplitude of the waves shows a gradual change toward the preshock level; if the amplitude was increased as a result of the shock, it becomes lowered. If, as is more often the case, the amplitude was diminished, it then gradually attains greater voltage. At the same time the irregularities in the wave forms and in the general "structure" of the electroencephalogram decrease, although the "disorganized" type of activity is still apparent. Slow potentials also become less frequent.

What may be described as the third phase of the record now sets in, approximately one and a half to four minutes after passage of the current, representing the transition period from abnormality to relative normality of the record and corresponding clinically to the period of diminishing confusion and the gradual development of "complete consciousness" in the patient. The occasional slow potentials disappear entirely, or at least return to the approximate frequency of occurrence which was noted prior to the passage of the current, while the disorganization and irregularity in the general wave pattern gradually diminish, soon to resemble or approximate the last preshock record. As a rule, the record attains the "normal" state in about five to ten minutes after administration of the shock. In some cases, just before the record becomes stabilized at the preshock level, one observes sudden marked diminution in the voltage output, which lasts about ten to fifteen seconds. It is quite possible that this change is associated with a sudden awareness of the environment on the part of the patient. At this stage the patient may be resting entirely quietly, with the eyes closed. In several instances the electroencephalographic pattern did not return to the "normal" until fifteen to twenty minutes after passage of the current. In 1 of these instances a continuous series of 3 cycle per second waves, with an amplitude of 30 to 50 microvolts, appeared for about fifteen seconds during the first phase. In the others the first phase of the record consisted in the appearance of many 4 to 7 cycle per second waves of relatively high voltage. In these cases there occurred what appeared to be relatively severe "petit mal" attacks, in which the patients remained unconscious or confused for a longer period than did the others. In addition, the electroencephalograms all exhibited, with 1 doubtful exception, a high voltage, high incidence alpha rhythm throughout the preshock phase. Patients having only a relatively mild, short "petit mal" attack and regaining complete consciousness in a relatively short period exhibited an electroencephalogram which returned to the normal status comparatively early. There seemed to be, therefore, some degree of correlation between the clinical severity of the attack and the character of the preshock record, on the one hand, and the degree and duration of abnormality of the electroencephalogram, on the other. No definite correlation could be noted between the different voltages used to produce the petit mal type of response and the electroencephalographic pattern.

It should be emphasized that not all of our records obtained simultaneously with the petit mal type of response can be definitely described in terms of the three phases mentioned. This is, of course, partially due to the variability in the pattern of response of the individual patients, even when only a minor attack results. It should be added that in no instances were the "spike and dome" wave patterns, described as typical for the epileptic petit mal attack,[4] observed. This is all the more interesting because of the similarity between the clinical manifestations of the "electric petit mal" response and the spontaneous epileptic petit mal attack.[2] Figures 2 and 3 illustrate electroencephalographic changes associated with the "petit mal" response.

B. *The Generalized Convulsion.*—In the generalized convulsions induced by the electric shock, the records obtained resembled in general patterns observed after other types of convulsions, such as those induced by metrazol [5] and those obtained immediately after spontaneous seizures in epileptic subjects. As already mentioned, it is extremely difficult to evaluate, for purposes of electroencephalographic study, the waves recorded during the actual seizure, since tonic and clonic muscular movements produce high voltage, high frequency action potentials which largely mask or prevent the recording of potentials originating in the brain. As soon as most of the muscular movements had ceased, toward the end of the clonic phase of the convulsion, wave patterns from the brain appeared on the recording tape. Brain potentials were obtained, therefore, only at the end of the seizure, which in the average case was from forty to sixty seconds after the application of the current to the head. We have chosen to discuss the postconvulsive electroencephalographic patterns in the light of three arbitrarily chosen clinical phases occurring immediately after each convulsion. The first phase, beginning immediately after all final clonic movements have ceased, consists of a variable period, usually from one to two minutes, of hyperpnea and stertorous breathing, cyanosis, frothing at the mouth, elevation of blood pressure and unconsciousness. Very often the period of apnea which occurs during the fit is prolonged for several seconds after cessation of clonic movements before stertorous breathing begins. During this first phase, the record at the onset shows practically no activity except for slow, irregular swings of the base line. Very low amplitude, slow

4. Gibbs, F. A.; Lennox, W. G., and Gibbs, E. L.: The Electroencephalogram in Diagnosis and in Localization of Epileptic Seizures, Arch. Neurol. & Psychiat. **36**:1225 (Dec.) 1936. Jasper, H. H., and Nichols, I. C.: Electrical Signs of Cortical Function in Epilepsy and Allied Disorders, Am. J. Psychiat. **94**:835, 1938.

5. Cook, L. C., and Walter, W. G.: The Electroencephalogram in Convulsions Induced by Cardiazol, J. Neurol. & Psychiat. **1**:180, 1938. Davis, P. A., and Sulzbach, W.: Changes in the Electroencephalogram During Metrazol Therapy, Arch. Neurol. & Psychiat. **43**:341 (Feb.) 1940.

potentials of 0.5 to about 2 cycles per second then appear, on which at times low voltage, high frequency waves (30 to 40 cycles per second) may be superimposed. This pattern occurs fairly equally, on both sides, over the entire cortex. The second phase, usually varying from two to five minutes, is characterized clinically by unconsciousness, but with gradual diminution to disappearance of the cyanosis, return of respiration to a more normal type and occasional involuntary movements of

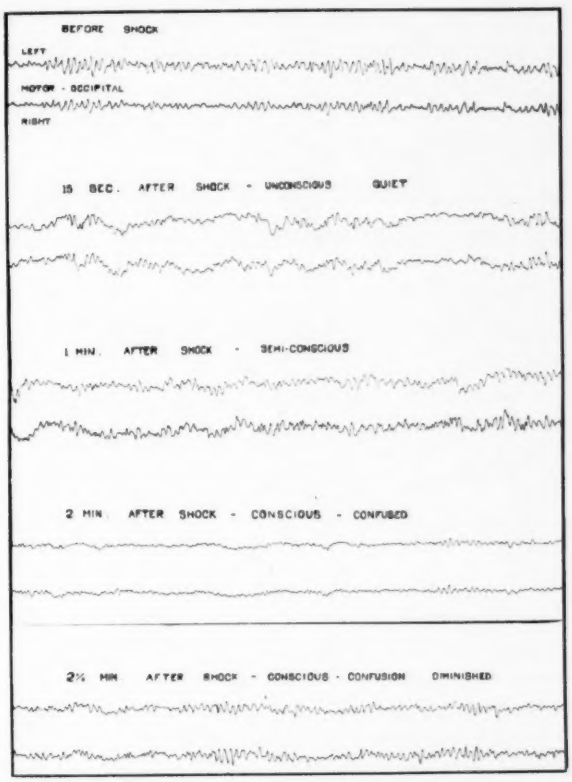

Fig. 2.—Electroencephalograms associated with the "petit mal" response. The preshock record in this case shows a relatively normal pattern. Note the marked irregularity in the pattern fifteen seconds after the administration of the shocking current. One minute after the passage of the current the record still shows some irregularity but, nevertheless, is returning to the preshock state. Note the rather sudden and marked diminution in the amplitude of the waves two minutes after the shock was administered, while approximately a half-minute later the record has returned practically to the preshock state.

the limbs. The record during this phase exhibits a gradually increasing amplitude of the slow potentials, an increase in their incidence and a

slight increase in frequency, so that 2 to 4 cycle per second waves now predominate. High frequency, low voltage waves may or may not be superimposed on the slow waves. Quite often, as more of the slow potentials appear in the record, they at first become grouped in short series of 3 or 4, with a zero potential line spaced between the groups for 2 to 5 second intervals, but as their incidence increases the groups of waves coalesce and form a continuous series of slow waves. In the third clinical phase the patient begins to come out of his unconscious state and at times may pass through a period of mild excitement and marked confusion before he becomes somewhat cognizant of his sur-

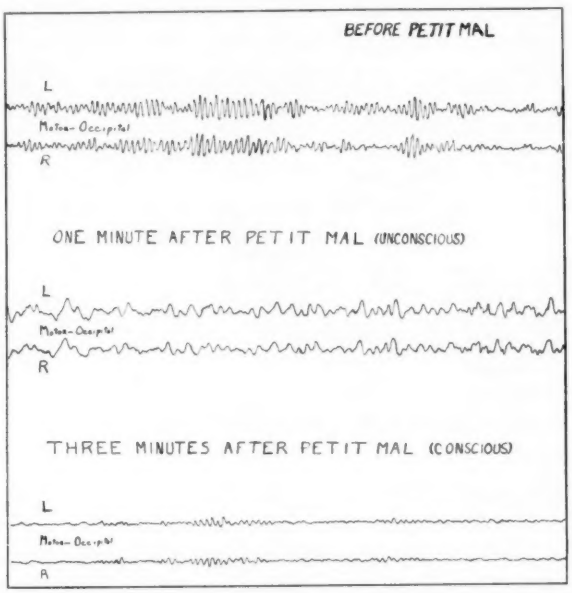

Fig. 3.—This is another variation of the pattern associated with "petit mal" attacks after administration of electric shock. Note the relatively high amplitude and incidence of the alpha rhythm in the preshock pattern. One minute after the attack there is fairly marked irregularity in the electroencephalographic pattern, with the frequent appearance of slow waves. Three minutes after the attack the record tends to return to the normal level.

roundings. Usually he regains "full" consciousness in five to ten minutes after the convulsion. The electroencephalogram in this period begins to show reappearance of the alpha waves noted in the preshock record. These may be superimposed on and interposed between the slow potentials. Often the alpha rhythm first makes its reappearance while the patient is still unconscious, a few seconds before he begins to exhibit signs of reawakening. Many slow potentials persist for some time after

the patient has regained "full" consciousness, but during the latter part of the third clinical phase the slow waves gradually increase in frequency, so that the record consists predominantly of 3 to 6 cycle per second waves of moderate to high amplitude. The rate at which the abnormal waves diminish in incidence and the length of time for which they persist in the record depend chiefly on the character of the preshock electroencephalographic pattern and the number of treatments the patient has already received. In general, a record which is essentially within normal

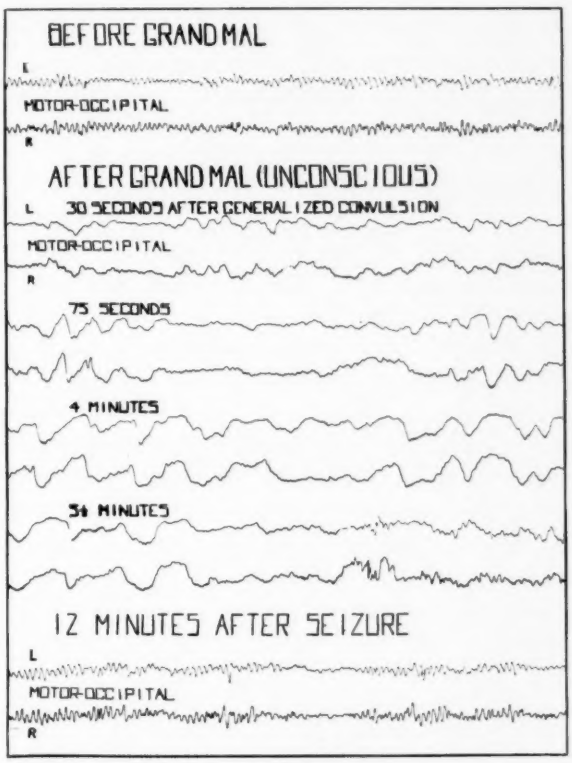

Fig. 4.—Electroencephalographic variations associated with an electrically induced generalized convulsive seizure. Note the relatively normal preshock pattern. Immediately after a "grand mal" attack few waves are noted in the record, which is characterized chiefly by an irregular or wavy base line. After one minute, with the patient still unconscious, definite slow waves of high amplitude appear in the record, at first in short series of 2 to 3 and then gradually becoming almost continuous. As noted in this case, twelve minutes after the seizure the record tends to approximate the preshock pattern.

limits prior to the convulsion returns to an approximately normal state in fifteen to thirty minutes after the seizure. The occipital and parietal areas, respectively, show a return to the normal rhythm first, and the

frontal regions, finally. If the preshock record exhibits irregularities or abnormalities, the record usually requires a somewhat longer period to return to the preshock level. It may be added that the amount of the voltage bears no definite relation to the degree of abnormality of the electroencephalogram, and incidentally none to the severity of the generalized seizure. Figure 4 illustrates electroencephalographic variations associated with a generalized convulsive seizure induced by an electric shock treatment.

II. CHANGES ASSOCIATED WITH SUCCESSIVE TREATMENTS

With successive treatments in which generalized convulsions have been produced, a period seems to be reached at which the physiologic state of the brain, as evidenced by the electroencephalogram, remains abnormal for a number of days, even though no further treatment is administered. This abnormality consists essentially in the frequent appearance of 3 to 6 cycle per second waves of moderate to high voltage, on which alpha and beta rhythms are often superimposed. These waves persist first in the frontal areas and then, with successive treatments, extend posteriorly all over the brain. Most striking at this stage is the appearance at infrequent and irregular intervals in the record of a sudden burst of continuous slow, high voltage waves, for an average period of from one to five seconds, very much resembling the "epileptic" or "convulsive" pattern in which the spike wave is absent and only the rounded wave forms occur in continuous series. Hyperventilation for a period not exceeding one minute always increases the per cent time occurrence of the slow potentials and frequently induces the sudden development of a "train" of the slow waves. The abnormal waves occur equally and fairly synchronously on the two sides. They may be obtained from all regions of the brain, as already mentioned, but appear initially and also exhibit their greatest amplitude over the frontal areas. This state of persisting abnormality in the electroencephalographic record is usually first noted after the patient has received a series of 3 to 5 generalized convulsions in a period of one to two weeks. The maximum change in the record, that is, the greatest degree of abnormality persisting for a period exceeding twenty-four hours after the last convulsion, as indicated by almost continuous series of slow, 3 to 6 cycle per second waves in all leads, usually appears at some time after the sixth to the twelfth convulsion. The length of time for which these abnormal electroencephalographic patterns persist varies to some extent, but depends mainly on the total number of convulsions induced in the individual patient and the frequency with which these treatments are administered. There does not appear to be any definite or consistent relation between the degree of clinical improvement per se and the electroencephalogram.

A statistical survey of our follow-up observations on these 61 patients, who were studied electroencephalographically for periods ranging from three to six months after cessation of therapy and who exhibited relatively normal pretreatment electroencephalograms, has indicated that the following generalizations are warranted in the usual case in which electric shock therapy is administered at the New York

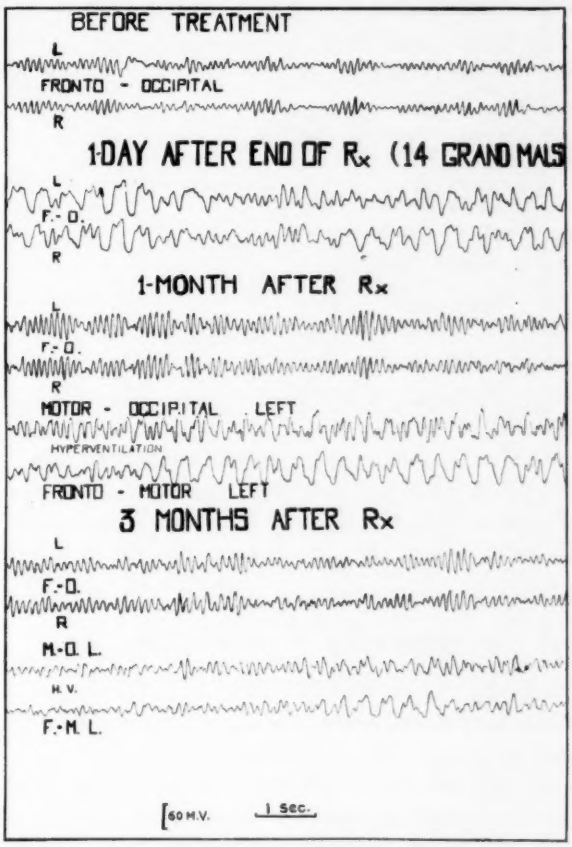

Fig. 5.—Electroencephalograms of a patient who was subjected to a relatively large series of convulsions during the course of treatment.

State Psychiatric Institute: 1. Patients who received 6 or less major seizure treatments exhibited electroencephalographic patterns in which abnormally slow waves completely disappeared in from one to five weeks. 2. Patients subjected to a series of from 7 to 12 convulsions showed records in which all abnormally slow waves disappeared after one to three months. 3. Patients who received 13 or more convulsion treatments (maximum number administered was 22) may be divided into

two groups: (*a*) Those whose encephalograms showed disappearance of abnormal slow waves two to six months after cessation of therapy. These patients constituted about 70 per cent of the entire group, and the majority received a series of 13 to 16 treatments. (*b*) Those whose records still showed persisting slow potentials, particularly from the anterior regions of the brain, at the end of six months, especially after

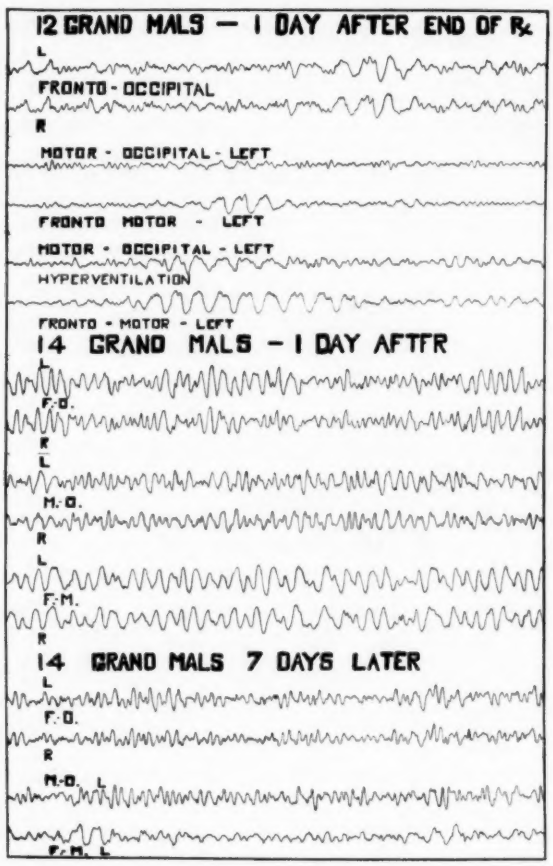

Fig. 6.—Electroencephalograms of a patient who was subjected to a relatively large series of convulsions during the course of treatment.

hyperventilation. These patients constitute the remaining 30 per cent of the group.

It is to be noted that we speak of our records as exhibiting disappearance of abnormally slow waves (those less than 8 cycles per second), and not as showing complete return to the normal, or to the pretreatment state. The reason for this lies in the interesting observation that many of the patients, particularly those who were subjected

to a series of 8 or more generalized convulsions, showed electroencephalograms characterized by an almost continuous high voltage, alpha rhythm, even present to a remarkable degree in anterior leads over the brain, which persisted in the records after all slow potentials had disappeared. The frequency of these waves was essentially the same as the alpha frequency of the pretreatment record; however, there appeared to be a marked reenforcement of the alpha activity, usually most pronounced in the electroencephalogram several weeks after termination of treatment. So far as we are aware at present, the presence or absence of this "reenforced" alpha rhythm some months after the end of therapy bears no definite relation to the degree of clinical improvement in the patient. Patients who were clinically completely recovered and, likewise, those who showed no improvement whatsoever exhibited similar patterns in this respect.

Several patients were subjected to a series of "petit mal" seizures only, without any generalized convulsions. None of these patients exhibited electroencephalographic abnormalities (slow potentials) which persisted for a period exceeding twenty-four hours, even after a course of 12 seizures had been given. Furthermore, "minor" seizures which were alternated with convulsions during the course of treatment seemed to have very little effect on the electroencephalogram except for the short-lived changes already described which were noted immediately after the attack but did not persist for any appreciable length of time. Figures 5 and 6 illustrate the variations in the electroencephalograms of patients who received relatively large series of convulsions during the course of their treatment.

COMMENT

The application of therapeutic electric shock to psychiatric patients has been associated in all cases studied so far with a change in the electroencephalographic pattern. If the shock results in a minor, or "petit mal," type of response only, "mild" and relatively transient changes are produced in the record. In our series these changes have in no case resembled the "spike and dome" pattern described by Gibbs and co-workers, Jasper and other investigators as typical of the epileptic petit mal seizure. Patients subjected to minor attacks alone during the course of their treatment have exhibited no definite persisting abnormalities in their electroencephalographic records, in the sense that no abnormalities remained in the records for a period exceeding twenty-four hours subsequent to the end of treatment. In those cases in which convulsions chiefly or entirely of the generalized type were induced, abnormalities in the electroencephalograms consisted mainly of 3 to 6 cycle per second waves of high amplitude which persisted for some time after the cessation of treatment. The length of time during

which this abnormal pattern persists after each individual seizure shows a tendency to increase with successive shocks until a stage is reached (usually after the sixth generalized convulsion) at which the abnormality may be evident for a number of weeks or months, depending, in part at least, on the total number of convulsions administered. Patients in whom were induced less than 8 generalized seizures, at a frequency of 3 seizures per week, in practically all instances showed a return of the electroencephalographic pattern to the pretreatment level after a few weeks. Those with more than 12 generalized convulsions in the course of treatment showed in the majority of instances persisting slow waves in their records, even for several months after cessation of treatment. In many of these cases, even after slow potentials were no longer apparent, the records were still characterized by a "strong," high voltage alpha rhythm, as compared with the pretreatment records. These patients have not as yet been followed for a sufficiently long period to determine whether considerable "weakening" in this type of alpha activity occurs.

Because of the development of what may be interpreted as abnormal electroencephalograms during the course of therapy, we feel that it is of considerable importance to check on the development of the abnormal record during treatment. This, of course, would require a preliminary electroencephalogram prior to the initiation of any therapeutic convulsion procedure. Indeed, such a preliminary test is highly desirable, for not all patients receiving electric shock treatment may show perfectly normal electroencephalograms prior to initiation of therapy. It was noted in 6 cases in which abnormal waves were found prior to therapy that the electroencephalographic records appeared to be much more "sensitive" to the electric shocks. "Maximum abnormalities" developed more rapidly and persisted for longer periods after administration of a series of treatments than did the abnormalities in cases in which the pretreatment records were normal and the patient was subjected to the same number of shocks. In addition, if the pretreatment electroencephalogram showed an area of increased abnormality as compared with other areas of the brain, that particular area apparently exhibited a lower threshold for development of persisting abnormality than did the other areas.

Examination of the pretreatment electroencephalograms may also be of considerable practical importance in interpreting any unusual clinical occurrence during or after the course of treatment. One young patient who exhibited a "convulsive" pattern, but no "spike and dome" waves, prior to therapy and who was neurologically normal, with no history of any type of seizure prior to therapy, received a series of 15 electrically induced generalized convulsions. Approximately six weeks after cessation of treatment the patient had a spontaneous generalized convulsion, the first in his life. Several weeks later another spontaneous seizure

occurred. The electroencephalographic activity continued to show a greater degree of "abnormality" than was noted prior to therapy. Knowledge of the pretreatment "convulsive potentials" of the patient, such as could be inferred from the pretreatment electroencephalogram, might be of considerable value to the clinician in interpreting possible, but rare, subsequent seizures.

One interesting point, namely, the possibility of utilizing the electroencephalographic record obtained during the progress of treatment as an index of sufficient therapeutic shocks, should be discussed. It has been mentioned that the "maximum abnormalities" noted in the records were obtained after there were induced, on the average, from 6 to 12 generalized seizures. Several inferences might be drawn from this observation. First of all, it might be assumed that if the "abnormal" electroencephalogram is an index of disturbance in the brain produced by electric shock or the convulsion or both, then once the maximum abnormality in the electroencephalogram is produced the maximum functional change in the brain has likewise been produced, and therefore no further treatment is indicated. This, of course, assumes, first, that the abnormality in the electroencephalogram is related quantitatively to the degree of disturbance produced in the brain by the treatment and, second, that the electroencephalogram and the associated functional changes are directly related clinically to the therapeutic status of the patient. We see no reason for either of these assumptions, except within certain limits. It would appear that perhaps the assumptions are true for the first 6 to 8 treatments, when considerable clinical change may be observed to parallel considerable change in the electroencephalogram and when the initial functional changes associated with the shock may parallel to a certain extent the changes in the electroencephalogram. There is no evidence, however, to show that beyond this initial phase of the total response the electroencephalogram reflects directly further functional changes in the cortex. The electroencephalogram seems to reach a state of saturation so far as manifestations of abnormal potentials at any one time is concerned. Our observations show definitely that the abnormal potentials persist longer the greater the series of generalized convulsive seizures administered. For practical therapeutic purposes, therefore, it would be extremely hazardous to assume that because the electroencephalogram had reached its "maximum point of abnormality" the functional change in the patient had done likewise. It would seem more justifiable, perhaps, at this stage of the therapeutic procedure to rely more on the general clinical status of the patient and to continue the administration of seizures while the patient continues to show clinical improvement. This policy would also appear to be justified by the fact that the electroencephalogram does not parallel, so far as the incidence of "pathologic changes" is concerned, the general

clinical status of the patient. It is a fact that the patient usually shows clinical improvement while the electroencephalograms become progressively more "pathologic," and therefore one cannot at present draw any conclusions as to the specific relation between the pattern of the electroencephalogram and the general clinical status of the patient. Further investigation concerning the relation of the degree of "pathologic alteration" in the electroencephalogram and certain aspects of the clinical status of the patient, such as "memory defect," will have to be carried out before the final word can be spoken. One might also mention in this regard that if 6 to 12 seizures, the usual number necessary for the development of maximum abnormalities in the electroencephalogram, were taken as the optimal number of seizures, then little therapeutic improvement might be expected if the series of seizures were prolonged. Those using this method in treatment of patients with dementia praecox have uniformly held, however, that in such patients improvement may not be manifested until the series of seizures is prolonged well above this number, even to more than 20 seizures.

One might also argue that since the maximum pathologic alteration in the electroencephalogram is noted in the usual case after 8 generalized seizures, prolonging the series of seizures above that point might result in serious damage to the brain, with subsequent harmful effects to the patient. Such a belief would rest, of course, on the assumption of a definite correlation between the degree of abnormality in the electroencephalogram and the degree of permanent, or irreversible, pathologic change in the brain and would further require the assumption that an intact nervous system is necessary for a "normal" clinical status. With regard to the last point, there are those who believe that the clinical improvement with such forms of therapy as electric shock may even be directly related to the degree to which certain pathologic changes are produced in the brain. Such a view, of course, requires further experimentation and observation before its acceptance is justified. With regard to the first assumption, that concerned with a direct relation between abnormality in the electroencephalogram and the degree of irreversible change in the nervous system, there is indeed evidence to show that such a direct correlation is not justified. It has been shown that abnormal potentials, of the type elicited in our records, in all probability originate from functionally disturbed tissue, but tissues which at least still function and have not reached a phase of permanent alteration. Nonfunctioning elements, such as might be expected if the electric shock therapy resulted in irreversible cell changes, would not be expected to manifest abnormal potentials, and indeed a considerable degree of irreversible changes in the nerve cells, resulting perhaps in even rather widespread destruction of cells, may be compatible with a relatively normal electroencephalogram once the permanent stage of destruction

is reached. Likewise, one cannot conclude that because most of the abnormal potentials disappear within several months after cessation of treatment the cortical changes underlying the abnormal potentials are therefore reversible. It is true that the electroencephalographic changes are to a large extent reversible, but this does not mean that any concomitant changes in nerve cells are likewise reversible. Therefore the authors feel, as has already been stated, that the best index to therapeutic procedure at present is the general clinical status of the patient, at least until such a time as direct association between abnormality of the electroencephalogram and undesirable abnormality of some other phase exhibited by the patient is established.

On the basis of the electroencephalograms alone and the similarity of the post-treatment records to those seen commonly in cases of clinical epilepsy, one might argue uncritically that the electric shock therapy has in effect produced a "convulsive state" in the patient, or at least the electrophysiologic basis for one. Such an argument of course assumes that similarity of electrophysiologic response is related to similarity or likeness of causation and would assume, therefore, that the postconvulsive records obtained from patients subjected to electric shock indicate the same basic electrophysiologic disturbance, and perhaps mechanism, as that assumed to exist in the spontaneous convulsive state. A clinical observation which would seem to cast considerable doubt on such a belief is the fact that spontaneous convulsive seizures subsequent to electric shock therapy have not been observed to occur in patients with normal pretreatment electroencephalograms. Another clinical observation in the same vein is that as the electric shock therapy proceeds increasing voltages are required to produce subsequent attacks, despite similar resistances. This would seem to be a point against any idea that the nervous system becomes "sensitized" to convulsive seizures by electric shock therapy, at least so far as the evidence of sensitization is considered to be the presence of abnormalities in the electroencephalogram. Observations to date do not indicate that "induced fits beget spontaneous fits" in persons with normal pretreatment electroencephalograms.

One might raise the interesting question whether any relation exists between the clinical condition for which the electric shock therapy was administered and the "vulnerability" of the electroencephalogram to the abnormal changes associated with the seizures. This is an exceedingly difficult problem to solve because of the lack of specificity of the electroencephalogram for the various mental disorders treated and also because of the wide variations existing in the criteria used to set up even the various clinical disorders under investigation. It would be of considerable interest, however, to determine whether the electroencephalograms of "schizophrenic" patients as a group were relatively

more "vulnerable" to the electric shock therapy in terms of the production of pathologic potentials than the electroencephalograms of another group, for example, patients of the "manic-depressive" type. Further studies are being continued along this line to determine whether any such relation exists.

SUMMARY

1. A group of 61 patients receiving electric shock therapy at the New York State Psychiatric Institute and Hospital were studied electroencephalographically. Over 350 records were obtained on this group of patients. Records were taken immediately after individual shocks, resulting either in "petit mal," or "minor," seizure response or in the generalized seizure response. In addition, the records were obtained at various stages during the course of treatment and at various intervals after cessation of the course of therapy, up to a period of six months.

2. Patients subjected to the "petit mal," or "minor," seizure type of treatment by the electric shock method exhibited only very temporary and transient changes in their electroencephalograms taken immediately after administration of the shocking currents. Large series of the "petit mal" type of treatments alone did not produce appreciable alterations in the electroencephalographic patterns, which persisted for a period exceeding twenty-four hours. In none of these instances was the "spike and dome" pattern, as described in cases of epilepsy, evident.

3. Patients subjected to the generalized convulsive seizure or to a series of generalized convulsions exhibited fairly marked changes in their electroencephalographic patterns, resembling in type those observed after convulsions produced by other means or occurring spontaneously. The larger the series of treatments administered, the more pronounced became the abnormalities and the greater the duration of time for which these abnormalities persisted.

4. In general, the electroencephalographic abnormalities associated with electric shock treatments are for the most part "reversible" in the sense that they gradually disappear. It should be stressed that this does not necessarily imply that any concomitant functional or histopathologic disturbances which may occur as a result of the treatments are also correspondingly "reversible."

5. Continued follow-up studies are being carried out on patients in whom were induced large series of convulsions and whose records after six months still exhibited abnormally slow potentials.

Miss Rhoda Bigelow gave technical assistance in applying the electrodes and in taking many of the records.

CHANGES IN THE BRAIN AFTER ELECTRICALLY INDUCED CONVULSIONS IN CATS

BERNARD J. ALPERS, M.D.
AND
JOSEPH HUGHES, M.D.
PHILADELPHIA

The widespread use of electrically produced convulsions for the treatment of mental disorders naturally gives rise to the question whether such artificially induced convulsive states are associated with evidence of damage to the brain. No observations on such changes in the human brain have as yet been published, to our knowledge. There has been an abundance of articles on the clinical, but none on the pathologic, features of induced convulsions. For this reason we have studied the brains of 30 cats in which artificial convulsions were produced by the electric current in order to determine, in animals at least, what change such convulsions cause in the nervous system.

MATERIAL AND METHODS

Thirty cats were given electrically induced convulsions (table). The first group, cats 1 to 6 inclusive, received a series of 23 shocks; these were given daily except Sundays. The second group, cats 7 to 15 inclusive, were given a series of 18 shocks; these were also given six times weekly. The third group, cats 16 to 30 inclusive, received 10 shocks and were treated three times weekly.

No hypnotic drug or anesthesia was required in order to carry out this procedure, as the animals remained friendly throughout the experiment. From this it was judged that they had an amnesia for the shocks similar to that which is experienced by patients.

The electric shocks were administered through small disk electrodes, about 5 mm. in diameter, which were held in place by a rubber band slipped over the cat's head. In order to insure good contact the underlying hair was cut away and electrode paste rubbed into the scalp.

The animals were shocked with a strength of current which was of threshold value for producing the convulsive seizure. The apparatus to deliver this current was the same as that used clinically in the treatment of patients. It consisted of a step-down and step-up transformer operated by an electrical timing switch

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From the Department of Nervous and Mental Diseases, Jefferson Medical College, and the Institute of the Pennsylvania Hospital.

and so designed that the duration of the shock, the voltage and the milliamperage could be varied at the will of the operator. The apparatus operated on a 110 volt, 60 cycle, alternating current. It was not possible to state exactly the strength of current acting on the brain because of technical difficulties attending any attempts to measure what portion of the current penetrated the skull and reached the brain tissue. A current of a strength varying from 150 to 200 milliamperes was applied to the scalp. It has been estimated that about 10 per cent or less penetrated the cortex.

Summary of Data on Cats Subjected to Electric Shock Treatments

Cat Number	Number of Treatments per Week	Number of Shocks	Number of Convulsions	Total Number of Minutes in Convulsions
1	6	23	15	10
2	6	23	19	13
3	6	23	22	10.5
4	6	23	23	35.5
5	6	23	20	25.5
6	6	23	22	16
7	6	18	18	3.4
8	6	18	18	2.5
9	6	18	18	4
10	6	18	18	3.5
11	6	18	18	3.8
12	6	18	18	18.5
13	6	18	18	6.5
14	6	18	18	10
15	6	18	18	10.2
16	3	10	10	2.5
17	3	10	10	5
18	3	10	10	6.5
19	3	10	10	6
20	3	10	10	4.5
21	3	10	10	4.5
22	3	10	10	5
23	3	10	10	4.5
24	3	10	10	6
25	3	10	10	5
26	3	10	10	5.5
27	3	10	10	5.5
28	3	10	10	5
29	3	10	10	5
30	3	10	10	5

After the shock the animals were rendered unconscious, immediately after which they went into a tonic and clonic type of convulsive seizure. Occasionally convulsive seizures did not occur.

The cats were killed by section of the carotid artery. The brains were placed in dilute solution of formaldehyde U. S. P. and were sectioned within a few hours after this fixation. Embedding was both in paraffin and in pyroxylin. Special blocks were taken for formaldehyde–ammonium bromide treatment. In every instance studies were made with toluidine blue, cresyl violet and hematoxylin and eosin; with ponceau B for fat, and with stains for myelin (Weil), microglia and astrocytes.

PATHOLOGIC CHANGES IN THE BRAIN

The cats were divided into two series, of 15 animals each. In group 1 were included cats which were thought to have received more than

the equivalent of the human dose employed for ordinary routine treatment. For comparison, a second group of cats (group 2) was studied, in which the doses of electricity and the number and duration of the convulsions more closely resembled the situation for human subjects.

CATS SUBJECTED TO EIGHTEEN OR MORE ELECTRIC SHOCKS (GROUP 1)

All parts of the cortex and the entire brain stem and cerebellum were studied in each of the 15 cats.

Meninges.—In all animals there was some degree of congestion of the pial vessels over the cerebral hemispheres. This was more marked in some cats than in others.

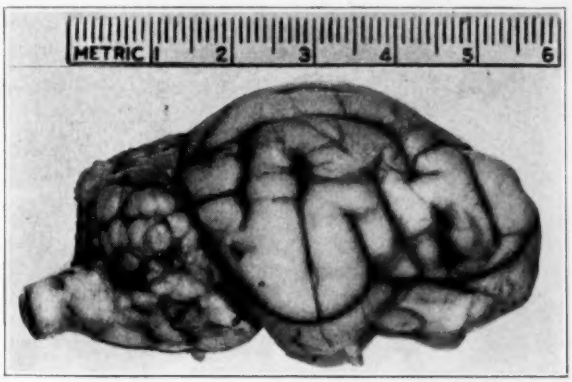

Fig. 1 (cat 2, second series).—Areas of hemorrhage in the subarachnoid space over the cerebrum and around the brain stem.

In 4 cats some degree of subarachnoid hemorrhage was observed. In 3 animals the hemorrhage was over the cortex and in 1 around the medulla. In all cases the hemorrhage was focal and confined to only a small part of the cortex. In 1 of the 3 cats with hemorrhage over the cortex the meningeal hemorrhage was on the mesial surface of one hemisphere. In 2 instances the hemorrhage was fresh, and in 2 others the red cells were disintegrated and hemosiderin granules were present. No damage to the adjacent pial vessels could be found.

In 3 of the 4 cats with subarachnoid bleeding there was some degree of fibroblastic proliferation in and around the hemorrhage. This undoubtedly represented efforts to organize the hemorrhage. This process was probably seen in its end stages in 2 other cats, both of which had focal areas of fibroblastic arachnoiditis. In 1 animal (cat 7) there were areas of thickened meninges here and there over the cortex. These areas were packed with fibroblasts, with resulting thickening of the

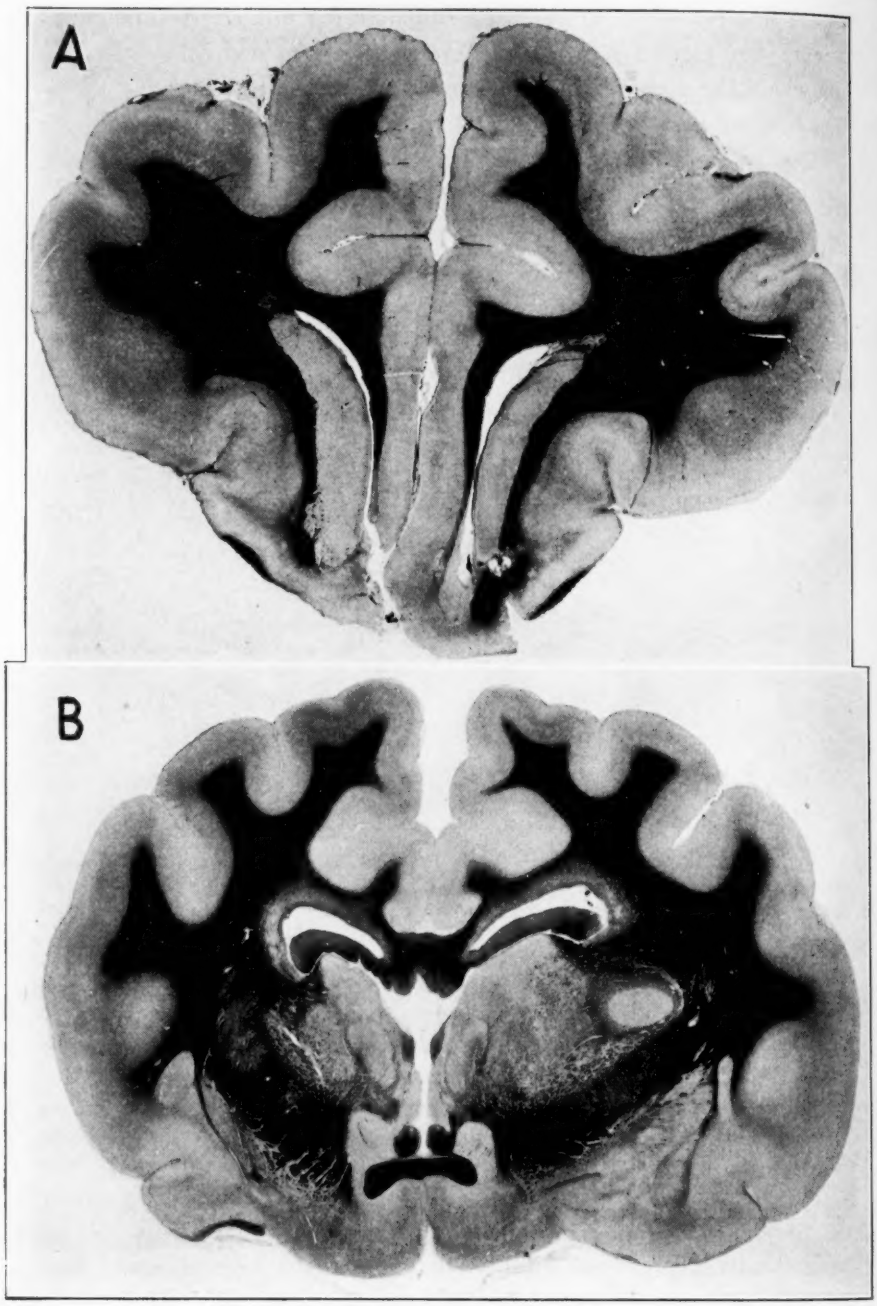

Fig. 2 (second series).—*A*, demyelination in the frontal area (cat 2); *B*, demyelination of the white matter around the lateral ventricles and in the internal capsule (cat 1).

arachnoid and firm adhesion of this membrane to the underlying cortex. This adherence was so strong in one area that the upper cortical layer was damaged and torn. In another animal (cat 8) there were scattered areas of mild fibroblastic thickening and arachnoiditis, but in one area of the cortex the arachnoid was greatly thickened and strongly adherent to the underlying cerebral cortex. It is quite probable that the changes in these 2 cats represent the end results of adhesive arachnoiditis in areas of subarachnoid hemorrhage.

Cerebral Cortex.—In all the animals the cortical architecture and the structure of the ganglion cells were normal. There was no loss of cells and no disturbance of the normal lamination of the cortex. The ganglion cells not only of the motor area but of the rest of the cerebral cortex showed no evidence of damage. This is in contrast to the reaction observed in experimental insulin shock and in metrazol convulsions.

In 1 animal (cat 3) there was a small focus of microglia cells and astrocytes in the frontal cortex. In another animal (cat 4) an extensive hemorrhagic infarct was observed in the white matter under the ependyma of the lateral ventricle. The tissue in this area showed only beginning dissolution. Red cells in moderate numbers lay free in the tissue. The microglia cells, oligodendrocytes and astrocytes in this area were swollen, but there was no gliosis.

The vessels in the cortex and the white matter showed no changes. Their endothelial linings were normal, and there was none of the congestion which was seen in the pial vessels.

Studies of the microglia cells, oligodendrocytes and astrocytes failed to reveal changes in any of these glia elements, except in the case of the hemorrhagic infarct.

Brain Stem and Cerebellum.—No changes were observed in the cells of the various nuclei in the diencephalon, mesencephalon, pons and medulla. The Purkinje cells of the cerebellum failed to show changes.

Summary.—Of the 15 cats in this series, 4 showed evidence of focal subarachnoid hemorrhage and 2 of adhesive arachnoiditis; 1 had a hemorrhagic infarct in the white matter, and 1 a glial nodule in the frontal cortex.

CATS SUBJECTED TO TEN ELECTRIC SHOCKS (GROUP 2)

In this group of 15 cats the number and duration of the convulsions simulated as closely as possible the conditions of treatment of the human subject.

Meninges.—Some degree of hyperemia was found in the meninges in all the animals. It consisted of scattered dilated and congested vessels and never involved all the meningeal vessels.

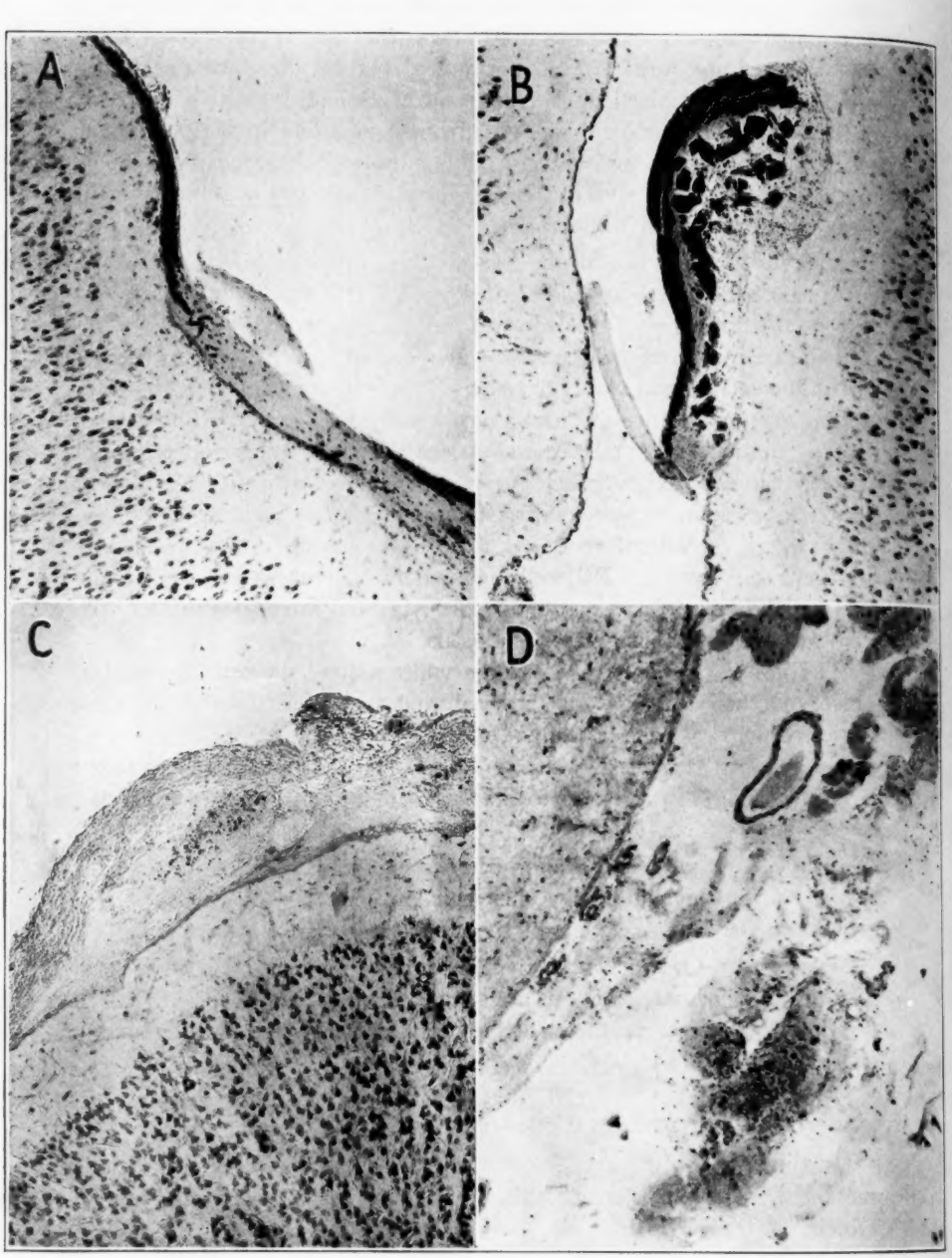

Fig. 3 (first series).—*A*, small area of subarachnoid hemorrhage over a cortical gyrus (cat 9); *B*, thrombosed vessel surrounded by hemorrhage on the mesial surface of the frontal lobe (cat 5); *C*, more extensive subarachnoid hemorrhage over a cortical gyrus (cat 1); *D*, hemorrhage in the meninges around the medulla.

In 10 of the 15 cats some degree of subarachnoid hemorrhage was observed. In 9 of these 10 cats the hemorrhage was slight and involved small areas here and there over the cortex. In 1 instance the sub-

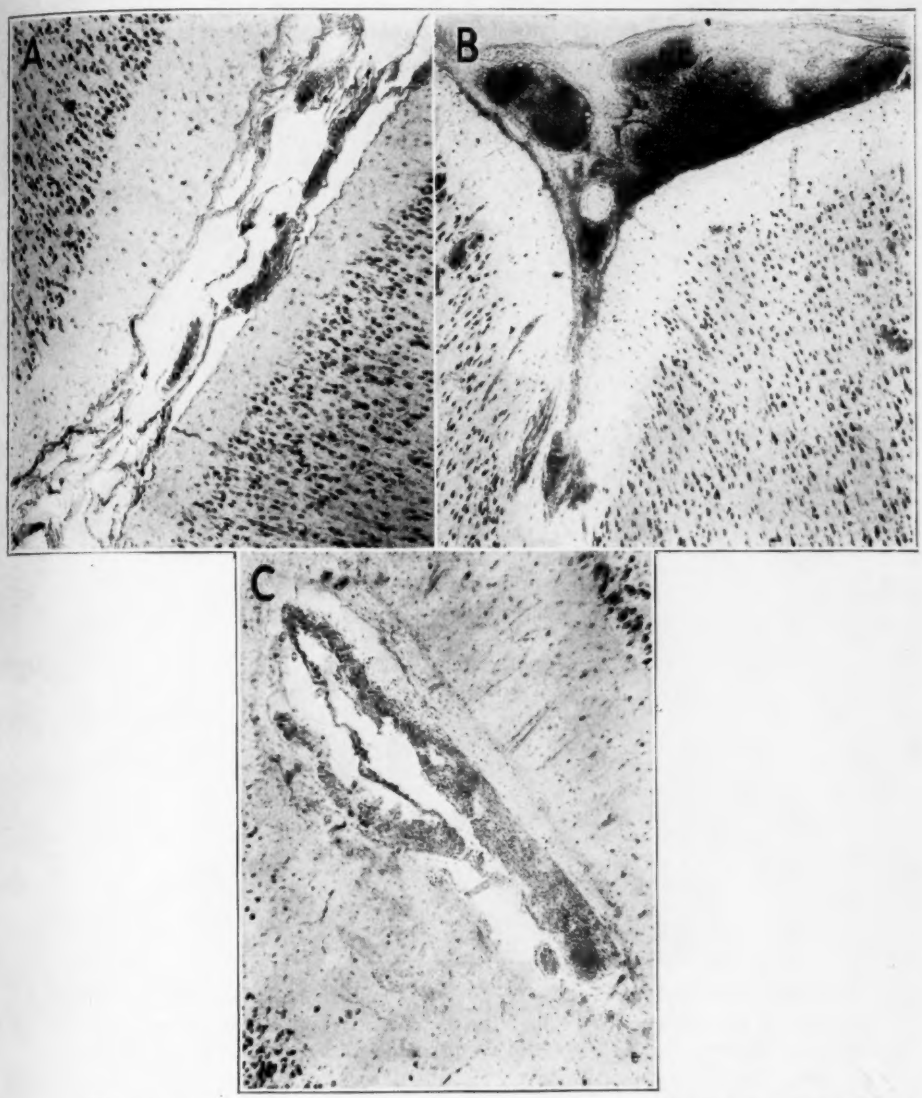

Fig. 4 (second series).—*A*, mild degree of hemorrhage in the subarachnoid space (cat 1); *B*, extensive subarachnoid hemorrhage and petechial hemorrhages in the cortex (cat 2); *C*, focal hemorrhage in the subarachnoid space (cat 6).

arachnoid hemorrhage was fairly large as to both extent and thickness. The blood in most of the cases was well preserved, but, as in the first series, areas of disintegrated red cells were seen. Slight efforts at

organization of the hemorrhage could be seen on the outskirts of the bleeding, but it was never great. There was no sign of damage to the meningeal vessels in any of the cats.

Cerebrum, Cerebellum and Brain Stem.—Punctate hemorrhages were seen in 8 of the 15 cats. These varied in number, size and distribution. They were never generalized or widespread, either in the

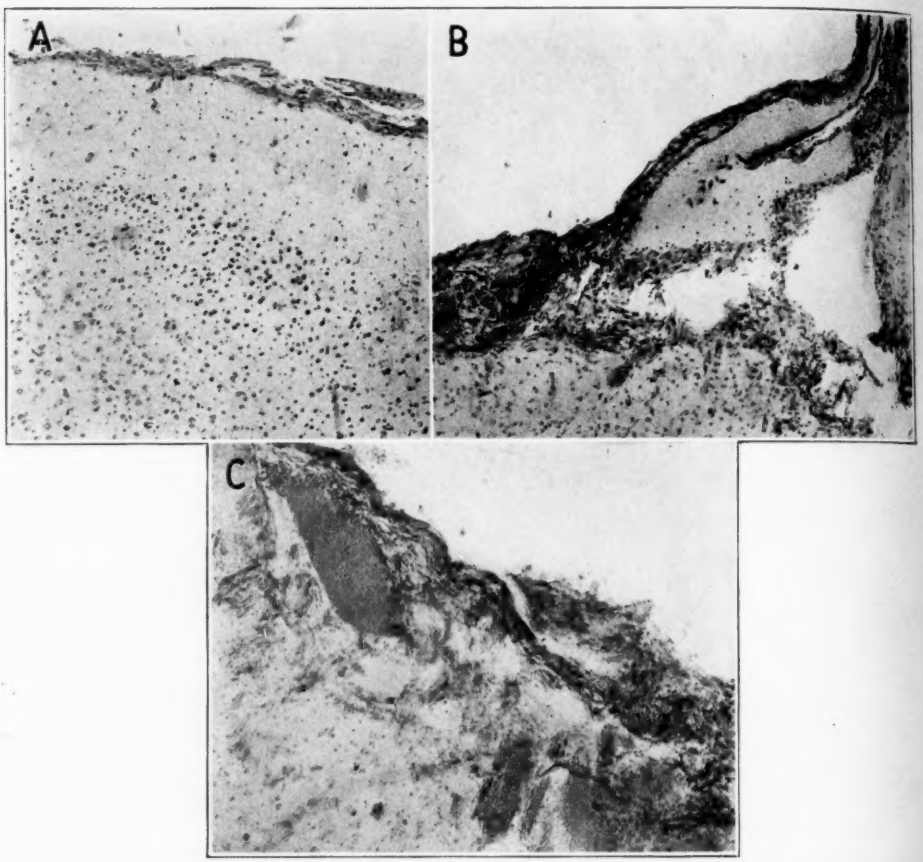

Fig. 5 (first series).—*A*, mild fibrosis of the pia-arachnoid (cat 8). *B*, marked fibrosis of the meninges over the cortex, with adhesion of the meninges to the cortex. Hemorrhage can be seen in the meninges to the left (cat 7). *C*, a similar process, showing organization of an area of subarachnoid hemorrhage, producing adhesive pia-arachnoid fibrosis (cat 8).

cerebral cortex or in the brain stem. As a rule, one found small groups of punctate hemorrhages in one part of the brain and either one or two similar groups elsewhere, or no further groups.

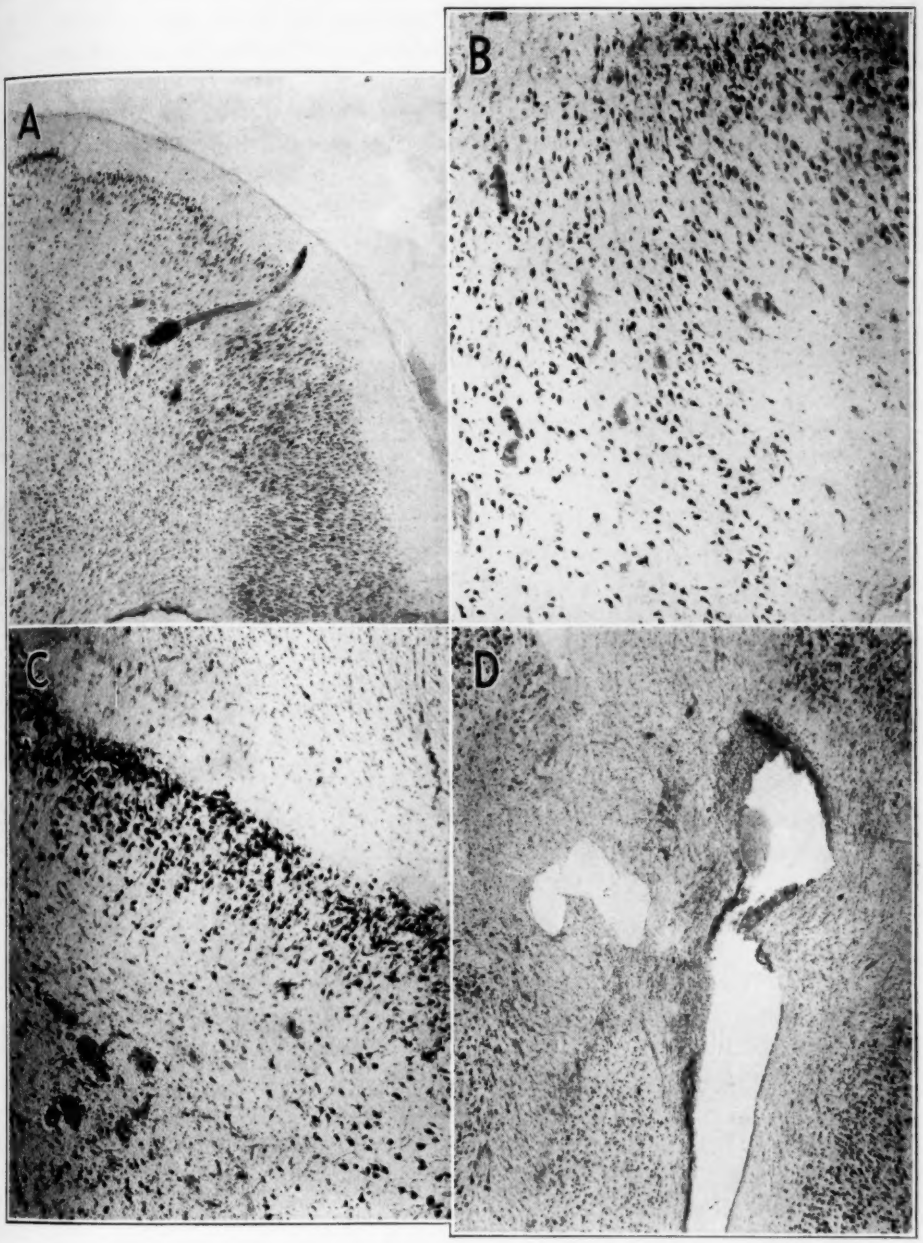

Fig. 6 (second series).—*A*, hemorrhages in the cortex, with a vessel leading down from the surface (cat 9); *B*, hemorrhages in the upper layers of the cortex (cat 2); *C*, hemorrhages in the cornu ammonis (cat 6); *D*, hemorrhage under the ependyma of the lateral ventricle (cat 3).

The hemorrhages were seen in the cerebral cortex, involving chiefly the frontal and temporal areas, in the subcortical white matter, in the region of the uncus, in the walls of the third ventricle, in the cerebellum, under the ependyma of the lateral ventricles and even in the third ventricle itself. Hemorrhage in the ventricle was observed in only 1 cat, but in this instance was rather extensive. No hemorrhages were seen in the medulla or pons.

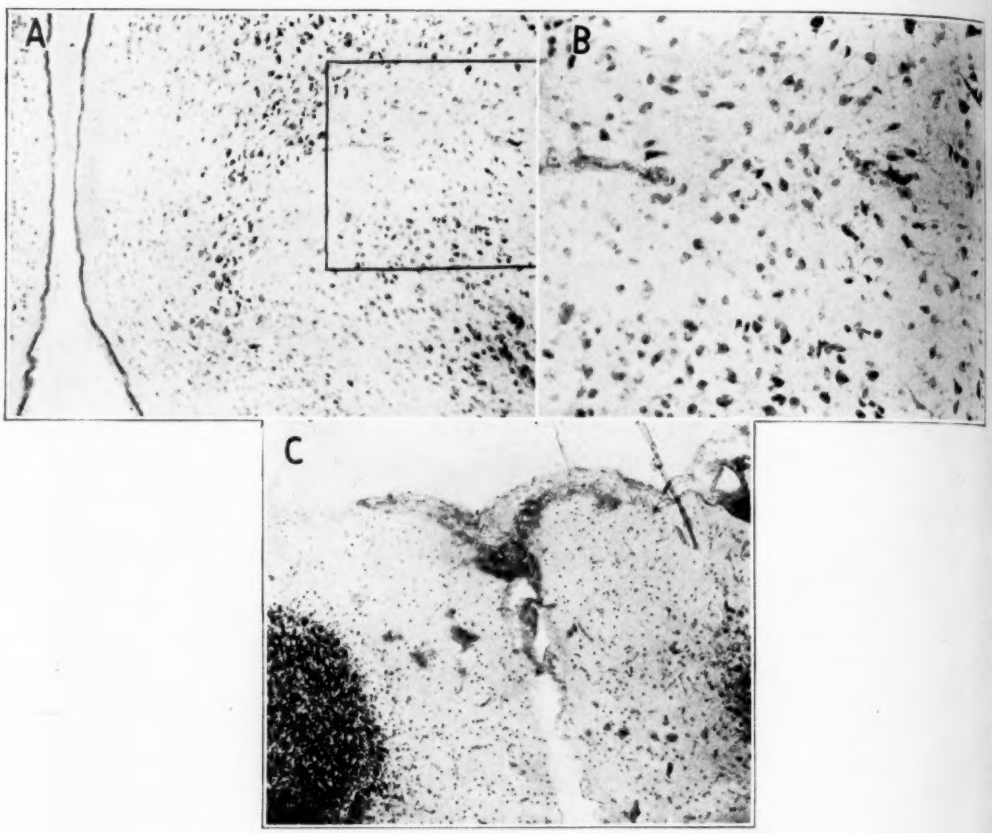

Fig. 7 (second series).—*A*, low power view, showing small hemorrhages outside the wall of the third ventricle (cat 2); *B*, high power magnification of the hemorrhages; *C*, small hemorrhages in the cerebellar cortex (cat 13).

The hemorrhages were typically punctate in 7 of the 8 cats, but in 1 (cat 2) the bleeding involved the surrounding brain substance and was rather extensive. The hemorrhages in all instances were fresh, and the red cells were well preserved. The perivascular character of the hemorrhages was easily apparent. Damage to the vessels was not found in most of the cases; in a few areas the vessel wall appeared to be torn,

but it was hard to determine whether or not this was the result of technical error. Microglial hyperplasia and hypertrophy were seen in the vicinity of some of the hemorrhages.

Myelin sheath stains revealed a breakdown of myelin and demyelination in some of the areas of more extensive hemorrhage.

The choroid plexuses of the lateral ventricles and the lateral recesses were greatly distended with blood.

In contrast to the punctate hemorrhages, the ganglion cells of the cortex, cerebellum and brain stem were remarkably well preserved. The Betz cells were fairly normal in appearance, save for a minor change in scattered cells, all of which were well within the limits of normal. Cells were, of course, destroyed in the region of the punctate hemorrhages, but apart from such areas the cells were surprisingly well preserved. Fat stains revealed no evidence of cell degeneration of a fatty nature. The basal ganglia, Purkinje cells and ganglion cells of the brain stem showed nothing. The microglia cells and astrocytes were for the most part normal except for occasional hyperplasia and hypertrophy of the microglia cells around some areas of hemorrhage. No disturbance of the cortical architecture was seen in any portion of the cortex, and no areas of cell loss were apparent.

Summary.—Of the 15 cats in this series, 10 had subarachnoid hemorrhage, and 8 showed hemorrhages of the brain, 7 of these being punctate and 1 more extensive. The ganglion cells were normal in appearance, and no damage to the vessels was apparent.

COMMENT

A survey of the observations on the 30 cats which received electric shock therapy reveals that damage to the nervous system is common in animals subjected to this form of treatment. Hemorrhage is the common lesion, particularly within the meninges and the brain substance. Of the 30 cats studied, 14 had subarachnoid hemorrhage and 9 hemorrhage within the brain substance itself. The subarachnoid hemorrhage was not as a rule extensive, except in a few instances. It was usually scattered over the cerebral hemispheres but in a few instances was found around the medulla. The hemorrhages within the brain substance were of a punctate character except in 2 instances, in 1 of which there was a hemorrhagic infarct and in the other a fairly extensive cerebral hemorrhage with hemorrhage into the ventricles. The hemorrhages varied widely in number and size from case to case. They were for the most part scattered, appearing in a single area of the cortex and nowhere else, or occurring as scattered punctate hemorrhages elsewhere in the brain or the brain stem. All parts of the brain appeared to be possible seats of the hemorrhage—the cerebral hemispheres, the cerebellum, the third ventricle and the hypothalamus.

There appears to be no apparent relation between the number of shocks and the changes in the brain. This is in agreement with the observations of Urquhart,[1] who found no relation between the severity of the shock and the presence of hemorrhage. In the second series of cats, which were subjected to many fewer electric shock treatments, there was a much greater incidence of hemorrhage within the brain than in the first series. Furthermore, there appears to be but little relation between hemorrhage and the total time of the convulsive seizures. Thus, in our first series of cats, an extensive hemorrhagic infarct was found in 1 animal (cat 4) in which the total time of convulsions was four minutes, while in another animal (cat 7) with a total of eighteen and a half minutes of convulsions only congestion of the pial and cortical vessels was noted. The same holds true for the animals in our second series. Cat 1, with a total of two and a quarter minutes of convulsions, showed rather extensive damage; cats 4 and 7, with five and six minutes of convulsions, showed less damage. It is not clear why some animals show evidence of hemorrhage in the meninges or brain while others fail to do so under similar circumstances. The possibility arises that there may be individual factors in each case which govern such reactions or that the circumstances attending the convulsions are not the same under all conditions. It seems fair to assume that while hemorrhage occurs with alarming frequency in experimental animals subjected to electric shock, it does not occur in all animals. From this it follows that if hemorrhage occurs in the human subject as a result of such treatment, it probably does not do so in every case.

The problem arises naturally as to the eventual fate of the hemorrhage. The animals studied were killed too early to answer this question definitely. In the case of the subarachnoid hemorrhage evidence was found to indicate that in the case of moderately extensive bleeding organization by fibroblasts took place, leading to adhesive arachnoiditis. This has possible clinical significance. As to the hemorrhages within the brain substance, these may in part be absorbed, or there may be replacement by glia and the formation of glial foci. Perivascular gliosis has been reported as a late sequel of electrical injury of the brain (Hassin[2]). Our animals were killed too soon, however, to observe the late effects of the hemorrhages. Among their more immediate effects must be mentioned the loss of the cells and fibers in the region of the extravasation.

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2. Hassin, G. B.: Changes in the Brain in Legal Electrocution, Arch. Neurol. & Psychiat. **30**:1046 (Nov.) 1933.

Of greatest importance, however, is the question whether similar changes in the brain may be assumed to be present in the human subject after electric shock treatment. No autopsy studies are as yet available for patients so treated. The necropsy reports on cases of human electrocution cannot be regarded as answering the problem, since the type of electrical current, usually a single severe shock of very high voltage, causes the death of the victim almost immediately. Jaffé [3] and Hassin have made thorough reviews of the changes in the human nervous system. While some investigators have reported that no changes were observed in the human brain after electrocution, others have found perivascular hemorrhages, especially in the medulla and the floor of the fourth ventricle. Hassin has reported large tissue tears, as well as tears of large blood vessels.

The conditions described in our animals have apparently been found previously in experimental animals exposed to various types of electrical injury with the object in mind of determining the reaction of the nervous system to the electrical current. In a large series of rats, Langworthy [4] observed hemorrhages in the nervous system, especially when using a high voltage (500 to 1,000 volts) alternating current, and much less frequently when using the continuous current. When voltages similar to those employed in our animals were used (110 volts) changes in the nerve cells were not prominent, but hemorrhages were still common. Similar hemorrhages have been found by Urquhart and by Morrison, Weeks and Cobb.[5] The last-mentioned investigators observed a greater tendency to hemorrhage with the alternating current. They found hemorrhages in the pia, the ventricles and the choroid plexus and pericapillary extravasation everywhere, especially in the basal ganglia and the medulla. The changes in the ganglion cells were mild when alternating current was used. Necrotic changes in the spinal cord with electric shock have been reported by MacMahon.[6]

The experimental conditions in many of these animals paralleled those used in electric shock therapy. It remains impossible to state, however, whether petechial and meningeal hemorrhages of a similar sort occur in the human subject. It is probably fair to assume that there is some damage to the human brain, the difference being one of degree rather than of kind.

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5. Morrison, L. R.; Weeks, A., and Cobb, S.: Histopathology of Different Types of Electric Shock on Mammalian Brains, J. Indust. Hyg. **12**:324 (Nov.); 364 (Dec.) 1930.

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CONCLUSIONS

Electrically induced convulsions were produced in 30 cats.

Subarachnoid hemorrhage, usually of mild degree but sometimes extensive, was found in 14 cats.

Hemorrhage in the brain substance (cerebral cortex and white matter, cerebellum, region of the third ventricle and third ventricle) was found in 9 cats, usually of a punctate type but more extensive in 2 instances.

Whether similar changes are to be expected in human beings treated with electric shock cannot be determined from this material.

DISCUSSION

Dr. M. T. Moore, Philadelphia: The authors' presentation is not only extremely interesting but of considerable importance because of the obvious implications with regard to the future of electrocerebral shock in the treatment of psychiatric conditions. The slides show hemorrhages not only within the subarachnoid space but in the parenchyma of the brain itself. Dr. Winkelman and I, during the past year, have subjected a series of cats to electrocerebral shock treatment analogous to that given to human subjects. The current has been carefully calibrated in terms of time, volts and milliamperes so as to produce a convulsive seizure similar to that induced in human beings. Our histologic observations on the brains of the animals studied are at variance with the authors'. We found no evidence of intracerebral or subarachnoid hemorrhage. At most, there appeared pyknosis of the ganglion cells of the frontal area lying beneath the frontal electrode. The spinal cords were entirely normal.

It must be borne in mind that excessive milliamperage may produce disruptive changes in brain tissue. I should like to ask Dr. Alpers whether the current used in his experiment was similar to that advocated by Cerletti and Bini and, also, what were the size and manner of placement of the electrodes?

Dr. Armando Ferraro, New York: The interesting report by Dr. Alpers and Dr. Hughes and the comments by Dr. Moore confront one with contradictory results, and I feel that the time is ripe for a concerted effort on the part of neuropathologists to discuss more closely the various factors involved in experimentally induced electric shock. If the constant changes observed by the authors in cats were to be reported in human material one should be hesitant in advising such a form of therapy. On the other hand, one is aware of the fact that from a clinical standpoint no appreciable ill effects have resulted from the application of electric shocks in hundreds of patients treated to date. I am wondering whether the duration of the passage of the current might not be one of the essential factors in explaining the difference between Dr. Moore's and Dr. Alpers' results.

EXPERIMENTAL PHARMACOLOGY OF POSTENCEPHALITIC PARKINSON'S DISEASE

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AND

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Despite the wide use of drugs in the treatment of Parkinson's syndrome, there is on the whole a lack of specific and objective data with regard to their effect on the two outstanding symptoms of the disease, namely, rigidity and tremor. The object of the present study was (1) to compare the effects of the drugs commonly used in management of the disease with those of a number of relatively new drugs and (2) to attempt better to understand the site of action of these drugs.

METHOD AND MATERIAL

Many pharmacologic observations were made on a number of patients with Parkinson's syndrome showing varying degrees of rigidity and tremor. Of these, 2 were finally selected as the most suitable subjects for intensive and prolonged study.

The first patient (S. I.), a woman aged 25, exhibited moderately marked rigidity of the right arm and leg, with mild tremor of these parts. She gave no definite history of encephalitis or other significant infection prior to the onset of the parkinsonian symptoms. These began when she was about 17 years old, progressed slowly and reached a stationary level at the age of 20. The slight tremor of her right arm and leg became aggravated when she was emotionally disturbed or unduly fatigued. Before the present study was begun, she had taken stramonium for several months, without improvement.

Neurologic examination on Nov. 3, 1940 disclosed the following signs: slight fixity of facies, moderate oscillating tremor of the tongue, moderate rigidity of the right elbow, marked rigidity of the right wrist and fingers of the right hand and moderate rigidity at the right knee, ankle and toes. The strength of the right hand, as measured by a dynamometer, was zero and that of the left 39 dynes. The fact that after administration of beneficial drugs the strength of the left hand always improved simultaneously with the improvement in strength of the right hand strongly indicated that though there were no manifest signs of parkinsonism

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on the left side, there was some obscure involvement of the left arm. When the patient walked, the right arm was held in a flexed attitude in front of her body and the right toes scuffed the floor. Writing was very slow and so tremulous that it was almost illegible.

The second patient (G. F.), an American woman aged 42, exhibited marked oscillating tremor of both arms and legs, with marked deformity contractures of the fingers, of the hands and of the wrists. She had had "sleeping sickness" for six months in 1919, associated with intense headache. In 1937 she began to show tremor, rigidity and weakness of all extremities, associated with slowness of motion, which steadily increased until she was unable to do her housework and became bedridden. She became irritable and showed changes in personality. In 1938 she became much worse and alternated between states of extreme drowsiness and outbursts of anger and screaming, so that finally commitment to a hospital for persons with mental disease became necessary.

Neurologic examination on Nov. 5, 1940 showed marked masklike facies; severe and constant oscillating tremor of the tongue and of both arms and legs, with disabling deformity contractures of the fingers of both hands and of the wrists; great rigidity of the neck, elbows, knees and ankles; extreme difficulty in gait, with the typical forward bending of parkinsonism; excessive secretion of saliva with constant drooling, and outbursts of yelling. Prior to the present study treatment with stramonium was tried, without favorable effect on her condition.

The following groups of drugs (table 1) were utilized: (1) sympathomimetic drugs, (2) parasympathomimetic drugs and (3) central stimulants. All drugs were given parenterally. Their effect was determined by the usual clinical tests for rigidity and speed of movements. Changes in strength were determined, when possible, by means of a hand dynamometer.

RESULTS

SYMPATHOMIMETIC DRUGS (TABLE 1)

1. *Epinephrine Hydrochloride.*—This drug was administered on several occasions to subjects S. I. and G. F. Its outstanding and invariable effect on S. I. was the production of a violent tremor of the right arm and leg after both intravenous and intramuscular administration. With intravenous injection of 0.001 to 0.01 mg. doses the tremor began within one minute and lasted for five minutes. With intramuscular injection of a 0.3 mg. dose these appeared in approximately three minutes and lasted fifteen to twenty minutes. With these doses no tremor of the left arm and leg appeared, except on two occasions when the tremor was unusually violent on the right side. Associated with the increased tremor and rigidity there were marked pallor of the face, a pounding sensation in the chest and marked elevation of the blood pressure, particularly after the intravenous administration of the drug. As the tremor developed, the right arm, wrist and leg became more rigid, and the right hand showed a corresponding decrease in strength, but as soon as the tremor stopped the strength of the right hand returned to its preadministration level. In subject G. F. epinephrine increased the tremor and the rigidity in all the extremities.

In an attempt to understand better the site of action of the drug, whether central or neuromuscular, 0.01 mg. of epinephrine hydrochloride was injected on two occasions into the right brachial artery of patient S. I. Within three minutes there developed a severe Raynaud-like attack: marked pallor and coolness of the hand and arm, tingling of

TABLE 1.—*Effect of Drugs on the Rigidity and Tremor of Parkinson's Syndrome (S. I.)*

Drugs	Dose (Intramuscular), Gm.	Ridigity	Tremor
Sympathomimetic			
Epinephrine hydrochloride	0.0003	Increased +	Increased +++
Ephedrine sulfate	0.04	No change	No change
Amphetamine sulfate	0.02	Decreased ++	Decreased or abolished
Dextroamphetamine sulfate	0.02	Decreased ++	Decreased or abolished
Levoamphetamine sulfate	0.02	Decreased +	No change
Neo-synephrin hydrochloride	0.01	Decreased +	No change
Propadrine hydrochloride	0.05	No change	No change
Paredrine	0.005	No change or slight increase	No change
P-methoxyamphetamine hydrochloride	0.02	Decreased +	No change
3,4-methylenedioxyamphetamine hydrochloride	0.02	No change	No change
Ergotamine tartrate	0.0005	Decreased +	No change
Parasympathomimetic			
Acetylcholine bromide	0.05-0.10	Decreased +	No change or slight decrease
Acetylbetamethylcholine hydrochloride	0.01	No change or slight increase	No change
Doryl	0.00025	Decreased +	No change
Furfuryltrimethylammonium iodide	0.005	No change or slight increase	No change
Prostigmine methylsulfate	0.0006-0.0012	Increased +	No change
Physostigmine salicylate	0.0006-0.0012	No change	No change
Scopolamine hydrobromide	0.0003-0.0006	Decreased +++	Abolished
Atropine sulfate	0.0006-0.0012	Decreased +	No change
Syntropan	0.01	No change	No change
Central Stimulants			
Caffeine with sodium benzoate	0.5-1.0	No change or slight increase	No change
Metrazol	1.0	No change or slight increase	No change
Coramine	0.5	No change	No change
Theophylline with ethylenediamine	0.5-1.0	No change	No change
Strychnine nitrate	0.0018-0.0036	No change	No change

the fingers and diminished volume of the radial pulse. This reaction reached its height five minutes after the injection and wore off in thirty minutes. After the first injection a mild tremor of the fingers, leg and foot occurred, lasting less than one minute, on the side of injection. After the second injection no tremor occurred, nor was there any change in the degree of rigidity in either instance. At the height of the attack

no general vascular reaction occurred, indicating that the action of the drug was either completely or almost completely confined to the arm.[1]

2. *Ephedrine Sulfate.*—In doses of 40 mg. given intramuscularly ephedrine sulfate had no influence on either the rigidity or the tremor.

3. *Amphetamine (Benzedrine) Sulfate in Aqueous Solution.*—In doses of 5 mg. given intravenously the aqueous solution of this drug effected a slight decrease in rigidity. Intravenous injections of 10 mg. produced a more definite decrease in rigidity, particularly in patient S. I., with corresponding increase in strength of the hands as measured by the dynamometer. With this dose the rigidity began to be affected within one minute after the injection, the maximum effect being reached within five minutes and the influence then gradually wearing off in forty-five to sixty minutes. With intravenous injection of larger doses, up to 30 mg., the loosening effect lasted two or more hours. After intramuscular injections of 20 mg. the effect on the rigidity began in approximately three minutes, the influence of the drug being maintained longer than that of the same dose given by the intravenous route and gradually wearing off in several hours.

Amphetamine (Benzedrine) Sulfate in Gelatin.—Amphetamine sulfate was also given in a vehicle of gelatin with the hope that its effects would be more prolonged. When it was administered in this vehicle intramuscularly in 20 mg. doses to subject S. I., the loosening effect manifested itself in about ten minutes, reaching its height in about twenty to thirty minutes, which was maintained for one hour and gradually wore off in about twenty-four hours, thus demonstrating that prolonged effect could be obtained by slowing up the absorption.

After the administration of amphetamine sulfate, a brightening effect occurred, in addition to the decrease in rigidity. With the larger doses, during the maximum effect of the drug, patient S. I. was able to hold the wrist and fingers in a normal attitude and gait showed definite improvement, with some swing of the affected arm. Marked improvement in writing occurred. During this period the patient was able to register a strength up to 40 to 50 dynes, with a corresponding increase in rapidity of movements of the wrist and fingers. At times when the rigidity was unusually reduced, the mild tremor which was usually present in S. I. disappeared. However, when the tremor was more marked it was not affected by even large doses of amphetamine sulfate. In subject G. F., a dose up to 30 mg. of amphetamine sulfate affected

1. Myerson, A.; Loman, J.; Rinkel, M., and Lesses, M. F.: Human Autonomic Pharmacology: XVIII. Effects of the Intra-Arterial Injection of Acetylcholine, Acetyl-Beta-Methylcholine Chloride, Epinephrine, and Benzedrine Sulfate, Am. Heart J. **16**:329-335 (Sept.) 1938.

the rigidity, so that the contracted fingers moved better, but there was no effect on the tremor. The drug was also without any effect on tremor in other subjects.

4 and 5. *Dextroamphetamine and Levoamphetamine Sulfate.*—These two isomers of amphetamine sulfate were compared with each other and with racemic amphetamine sulfate in the same dose. Both drugs decreased the rigidity, the dextro isomer much more effectively than the levo isomer. With intravenous injections of the smaller doses, 5 to 10 mg., this difference was not great but was very marked with intramuscular administration of doses of 20 mg. The latter dose of dextroamphetamine sulfate was as effective as the same dose of a racemic compound. Its effect on the mood seemed equal to that of the latter drug. Neither isomer influenced tremor.

6. *Neo-Synephrin Hydrochloride.*—After the intramuscular administration of 5 to 10 mg. of this drug there was a decrease in rigidity for approximately fifteen minutes. With the larger doses there was a moderate increase in blood pressure. The larger doses were not more effective than the smaller ones in their influence on the rigidity. The tremor remained unaffected. No effect on the mood was noted.

7. *Propadrine Hydrochloride.*—This drug (diphenyl-1-amino-2-propanol-1-hydrochloride) was administered intravenously in doses of 50 mg. Neither rigidity nor tremor was affected.

8. *Paredrine.*—Paredrine (p-hydroxy-α-methylphenethylamine hydrobromide)[2] was given by the intravenous route in doses of from 2.5 to 10 mg. With the latter dose marked increases of blood pressure occurred, frequently associated with severe headache. With the larger doses the rigidity was only slightly increased. There was no effect on tremor.

9. *P-Methoxyamphetamine Hydrochloride.*—This drug was given by the intramuscular route in 20 mg. doses. Slight to moderate decrease in rigidity usually occurred, appearing within five minutes, reaching its height in about ten minutes and then gradually wearing off in approximately two hours. Uncomfortable side effects usually followed its administration, namely, a feeling of general weakness and dizziness. These effects frequently lasted for several hours. The blood pressure showed a moderate increase, reaching its maximum in about twenty minutes and disappearing in one half hour. There was no effect on tremor.

10. *3,4-Methylenedioxyamphetamine Hydrochloride.*—No change in rigidity or tremor was observed after the intramuscular injection of this drug in 20 mg. doses. A feeling of weakness and general discomfort, lasting about one hour, was usually present.

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2. Paredrine was used in a concentration of 20 mg. per cubic centimeter of solution.

11. *Ergotamine Tartrate.*—This drug, given by the intravenous route in doses of 0.06 and 0.5 mg., effected a slight to moderate decrease in rigidity, associated with a corresponding increase in strength. These effects were more marked in S. I. than in G. F. The larger doses were not more effective than the smaller doses. The tremor was unaffected.

PARASYMPATHOMIMETIC DRUGS (TABLE 1)

1. *Acetylcholine Bromide.*—After intramuscular administration of 50 to 150 mg. of this drug to subject S. I., there was on several occasions a slight to moderate decrease in the rigidity of the right wrist. This change was associated with a corresponding increase in strength. These effects occurred within two minutes, reaching their height in approximately ten minutes, and wore off within thirty minutes. On other occasions there was no definite effect on rigidity or strength. When the drug was administered in doses of 10 mg. into the brachial artery of subject S. I., there developed marked flushing of the hand and forearm, associated with sweating of these parts. There were no general effects. During this reaction the rigidity and tremor were unaffected. In subject G. F. intramuscular injection of doses of the drug up to 200 mg. were without effect on the tremor or the rigidity.

2. *Acetylbetamethylcholine Hydrochloride* (mecholyl chloride).—This drug, when given in subcutaneous doses of 5 to 10 mg., sufficient to produce marked peripheral autonomic reaction, including marked flushing, sweating of the face and lowering of the blood pressure, effected either no change or a slight increase in rigidity. The tremor was uninfluenced.

3. *Doryl.*—When doryl (carbaminocholine chloride) was given intramuscularly in doses of 0.25 mg., a definite, though not marked, decrease in rigidity occurred within two minutes, the effect reaching its height in five minutes and finally wearing off in approximately one-half hour. When the drug was given in doses of 0.5 mg., the discomfort to the patient was very marked: flushing, salivation, perspiration and abdominal cramps, associated with a slight increase in rigidity of the affected parts.

4. *Furmethide.*—When administered intramuscularly in doses of 5 mg., this drug (furfuryltrimethylammonium iodide), which shows many effects similar to that of mecholyl and acetylcholine, produces a slight increase in rigidity. The effects wore off in about twenty minutes. The larger doses produced a secondary reaction, consisting of chilling of the skin associated with general tremulousness.

5. *Prostigmine Methylsulfate.*—With intramuscular doses of 0.6 to 1.2 mg., a slight to moderate increase in rigidity, lasting about one hour, occurred. There was no effect on the tremor.

6. *Physostigmine Salicylate.*—In doses of 1.2 mg., given intramuscularly, no definite alteration in the rigidity or tremor was observed.

7. *Scopolamine Hydrobromide.*—In doses of 0.3 mg., given intramuscularly, this drug was very effective in decreasing the rigidity in subject S. I. within ten to fifteen minutes after its administration, the effect lasting several hours. In this subject the beneficial effect of the drug was frequently prolonged for twenty-four to forty-eight hours. The decrease in rigidity preceded the drowsiness and a feeling of general muscular weakness. Intravenous injections, in doses as small as 0.08 mg., were markedly effective on the rigidity of patient S. I., the action manifesting itself within a few minutes and lasting approximately two hours. In subject G. F. the tremor was overcome fifteen to twenty minutes after the intramuscular administration of the drug in a dose of 0.3 mg. and did not recur for about three hours. This result was obtained day after day for several weeks. This beneficial effect was associated with diminution in the rigidity of the arms, and the patient was able to move the hands better. Her gait improved greatly during this period. Scopolamine, however, failed to influence the tremor of this patient when it was administered by mouth in doses four times the size of the effective intramuscular dose.

After several months of scopolamine therapy, subject G. F., who was emaciated and very weak before the treatment was begun, improved markedly in her general appearance and gained 23 pounds (10.4 Kg.). In other subjects the drug had a variable effect on tremor and rigidity. When doses larger than 0.6 mg. were given parenterally to several of these subjects, the undesirable side effects did not warrant its continuation, although a decrease in tremor and rigidity resulted.

The effectiveness of scopolamine was not prolonged when given in a gelatin vehicle.

8. *Atropine Sulfate.*—This drug, given in doses of 0.3 to 1.2 mg., was much less effective in overcoming the rigidity than was scopolamine or amphetamine. The effect on the rigidity in S. I. manifested itself within five minutes and lasted a variable length of time, in the larger doses as long as one to one and a half hours. The tremor was not influenced. When repeated doses were given, sufficient to increase markedly the pulse rate, the effectiveness of the drug was not appreciably increased. In subject G. F. the effect on rigidity was less than that in subject S. I. and there was no effect on the tremor.

9. *Syntropan.*—This drug, when given intravenously in doses of 0.005 mg., was without effect on either the rigidity or the tremor. At times with doses of 0.01 mg. the rigidity in S. I. was slightly increased.

CENTRAL STIMULANTS (TABLE 1)

1. *Caffeine with Sodium Benzoate.*—This drug, given intravenously in doses of 0.5 to 1 Gm., either did not affect or only slightly increased the rigidity. There was no effect on the tremor.

2. *Metrazol.*—Slow intravenous injections of this drug in doses up to 0.5 Gm. had either no effect on or slightly increased the rigidity. There was no change in the tremor.

3. *Coramine.*—Intravenous injections of 3 to 5 cc. of coramine (a 25 per cent solution of pyridine betacarbonic acid diethylamide) were without effect on either the rigidity or the tremor.

4. *Theophylline with Ethylenediamine.*—Intramuscular injections of this drug in doses up to 15 Gm. did not change the degree of rigidity or tremor.

5. *Strychnine Nitrate.*—Intramuscular injections, in doses as large as 0.18 mg., were without effect on either the rigidity or the tremor.

COMBINATION OF DRUGS (TABLE 2)

The following results refer to subject S. I. unless otherwise noted:

1. *Epinephrine and Acetylcholine.*—When epinephrine hydrochloride in doses of 0.3 mg. was administered simultaneously with acetylcholine bromide in doses of 100 mg., both drugs being injected intramuscularly, there was a slight tremor lasting for one to two minutes, in contrast to the marked tremor lasting fifteen minutes produced by the same dose of epinephrine hydrochloride alone. Only slight increase in the rigidity resulted. There were present the flush produced by acetylcholine and the pounding of the heart usually caused by epinephrine when either of these drugs is given alone. When an injection of acetylcholine alone was given after disappearance of the effects of the two drugs together a slight decrease in rigidity of the affected muscles usually occurred.

2. *Epinephrine and Scopolamine.*—When scopolamine was administered twenty to thirty minutes prior to injection of epinephrine hydrochloride a tremor did not result, although the other effects of the drugs were present. Not only did scopolamine prevent the tremor of epinephrine, but it exerted its usual favorable effect on rigidity. Intravenous injection of 0.15 mg. of scopolamine hydrobromide prevented the tremor-producing effect of epinephrine hydrochloride when the latter drug was later given intravenously in two successive doses of 0.01 mg. Similar results were obtained when both drugs were given intramuscularly: scopolamine hydrobromide in doses of 0.6 mg. and epinephrine hydrochloride in doses of 0.3 mg. In patient G. F. scopolamine overcame the spontaneous tremor in the usual manner, despite the later administration of epinephrine.

3. *Epinephrine and Amphetamine Sulfate.*—When epinephrine was given after amphetamine sulfate (in gelatin or aqueous solution), the rigidity-reducing effect of the latter drug was overcome and a tremor was produced. When the effects of the epinephrine wore off, the usual favorable effect of the amphetamine sulfate on rigidity manifested itself.

4. *Epinephrine and Atropine.*—The characteristic tremor associated with an increase in rigidity was produced by epinephrine hydrochloride when given after large doses of atropine sulfate (0.6 to 1.2 mg.). This reaction was later followed by a slight decrease in rigidity.

TABLE 2.—*Effect of Combinations of Drugs on the Rigidity and Tremor of Parkinson's Syndrome (S. I.)*

Drugs	Rigidity	Tremor
Epinephrine and acetylcholine	No change or slightly increased	Increased +
Epinephrine and scopolamine	Decreased +++	Prevented
Epinephrine and amphetamine sulfate	Increased +, then decreased ++	Increased +++
Epinephrine and atropine	Increased +, then slightly decreased	Increased +++
Epinephrine and ergotamine	No change, then slightly decreased	Increased +++
Epinephrine and doryl	Slightly decreased	Increased +++
Amphetamine sulfate and scopolamine	Decreased +++	Abolished
Amphetamine and atropine	Decreased ++	Decreased or abolished
Scopolamine and caffeine	Decreased +++	Abolished
Atropine and doryl	Decreased +	No change
Atropine and acetylcholine	Decreased +	No change or slight decrease
Prostigmine and acetylcholine	No change, then increased +	No change
Prostigmine and scopolamine	Decreased +++	Abolished
Prostigmine and amphetamine sulfate	Decreased ++	No change or slight decrease
Prostigmine and atropine	No change	No change

5. *Epinephrine and Ergotamine.*—Whether ergotamine tartrate was given simultaneously with or before the epinephrine, the characteristic tremor of epinephrine was produced, the relaxing effect of ergotamine manifesting itself when the epinephrine reaction disappeared.

6. *Epinephrine and Doryl.*—When doryl was given intravenously in doses of 0.25 mg. before intramuscular injections of 0.3 mg. of epinephrine hydrochloride, the tremor was not prevented, but a slight decrease in rigidity was produced. The hemodynamic effects of epinephrine were unaffected.

7. *Amphetamine Sulfate and Scopolamine.*—When amphetamine sulfate in gelatin was given intramuscularly in 20 mg. doses, together with intramuscular injections of 0.6 to 0.3 mg. of scopolamine hydrobromide, the rigidity-decreasing effect of the latter drug was not enhanced. The drowsiness produced by scopolamine was, however,

definitely diminished, while the general feeling of weakness did not appear to be affected. When the amphetamine was given at the height of the scopolamine effect, the drowsiness appeared to be affected in a more clearcut manner than when amphetamine was given at the same time as scopolamine. Similar effects were observed in patient G. F.

8. *Amphetamine Sulfate and Atropine.*—The combined effect of atropine sulfate (0.6 mg. given intramuscularly) and amphetamine sulfate (20 mg. given intramuscularly) was not greater than the effect of amphetamine sulfate given alone. The effect of these two drugs given together was less than that of scopolamine given alone.

9. *Scopolamine and Caffeine with Sodium Benzoate.*—When caffeine with sodium benzoate (0.5 Gm.) was given with scopolamine hydrobromide (0.3 mg.) by the intramuscular route, the usual effects of the former drug were produced. The drowsiness was not influenced by the caffeine.

10. *Atropine and Doryl.*—When doryl (0.25 mg. given intramuscularly) was combined with atropine sulfate (0.6 mg. given intramuscularly), the effectiveness of the former drug seemed to be only slightly increased.

11. *Atropine and Acetylcholine.*—Acetylcholine bromide in 50 to 100 mg. doses given at the height of the atropine effect appeared slightly and temporarily to enhance the effect of the latter drug.

12. *Prostigmine Methylsulfate and Acetylcholine.*—Acetylcholine bromide (50 mg.) administered intramuscularly twenty to thirty minutes after intramuscular injection of prostigmine methylsulfate (0.5 mg.) diminished the effect of the latter drug on rigidity. When the acetylcholine effect wore off, the full rigidity-producing influence of prostigmine methylsulfate was established. When a large dose of prostigmine methylsulfate (1.0 mg.) was followed by a large dose of acetylcholine bromide (200 mg.), the peripheral autonomic effects of acetylcholine, that is, flushing, salivation and prespiration, were extremely marked. This was associated with a slight increase in rigidity, but there was no effect on the tremor.

13. *Prostigmine Methylsulfate and Scopolamine.*—When these two drugs were given in the usual effective doses, the rigidity-reducing effect of scopolamine was as marked as when given alone. The tremor disappeared as usual.

14. *Prostigmine Methylsulfate and Amphetamine Sulfate.*—These drugs combined resulted in a decrease in rigidity in the degree usually produced by amphetamine sulfate alone. There was either no change or a slight decrease in the tremor.

15. *Prostigmine Methylsulfate and Atropine.*—These two drugs practically neutralized each other so far as rigidity was concerned.

COMMENT

That epinephrine produces adverse effects on tremor and rigidity by central action is indicated by the observation that these effects occur when the drug enters the general circulation but not when confined to the affected muscles (after intra-arterial injection).

The failure of acetylcholine, given either by the intramuscular or by the intra-arterial route, to influence rigidity or tremor strongly indicates that this chemical substance plays no role in the produciton of either symptom. On the contrary, that acetylcholine acts centrally is suggested, first, by the observation that the drug had on occasion a favorable, though mild, influence on the rigidity, and, second, that it diminished the severity of the tremor produced by epinephrine. When large doses of acetylcholine were reenforced by the previous administration of large doses of prostigmine methylsulfate, the rigidity produced by the latter drug was slightly enhanced. This result may be explained by the presence of the marked peripheral autonomic disturbances, with their attendant emotional effects, which probably overcome the mild central action of acetylcholine when given alone. The slight increase in rigidity produced by acetylbetamethylcholine and large doses of doryl may be similarly explained. On the other hand, small doses of doryl, insufficient to produce discomfort, effected a slight decrease in rigidity.

It is obvious that the action of drugs on the parkinsonian rigidity and tremor cannot be predicted on the basis of their autonomic classification and structural formulas. Thus, amphetamine sulfate and its isomers, neo-synephrin and p-methoxyamphetamine hydrochloride, diminish rigidity, while paredrine has either no effect on or slightly increases rigidity. Ephedrine, propadrine hydrochloride and 3,4 methylenedioxyamphetamine hydrochloride do not influence this symptom. Of the parasympathomimetic drugs, none compares with amphetamine sulfate and its dextro isomer in favorably influencing rigidity. Doryl in small doses and acetylcholine have slight rigidity-decreasing effects. Prostigmine methylsulfate has a definite, though not marked, rigidity-increasing effect, probably through direct action on the muscles. Physostigmine, given in the same dose as prostigmine methylsulfate, fails to influence the rigidity.

Of the two commonly used drugs scopolamine and atropine, the former is the much more effective. Scopolamine has a marked influence not only on the spontaneous tremor of parkinsonism but also on the tremor produced by epinephrine. Atropine, even when given in very large doses, was ineffective on either type of tremor and was much

less effective than scopolamine in influencing the rigidity. The difference in effectiveness of the two drugs is probably due to the fact that scopolamine is the more powerful centrally acting drug. Syntropan, structurally related to atropine, has a negligible effect on rigidity and tremor, probably because of its weak central action.

A discussion of the more exact sites and mechanisms of action of these drugs must be largely speculative. Suggestive answers to this complex question may be hazarded from some of the observations made in this study. Although such drugs as caffeine, metrazol, coramine, strychnine and amphetamine sulfate are all central stimulants, it is obvious that their central action varies in degree or in locus, as suggested by their effects on parkinsonian symptoms.

The effect of amphetamine sulfate on mood, on the normal sleep mechanism, on narcolepsy and on parkinsonian rigidity suggests an important stimulating action of this drug on subcortical structures, including the hypothalamus and the basal ganglia. That the site of action of the centrally acting sympathomimetic amines is subcortical is strongly suggested by the experiments of Morita,[3] who found that ephedrine, among other compounds, aroused decorticate dogs from light narcosis induced by chloral hydrate. Since amphetamine sulfate does not influence the tremor of Parkinson's syndrome, except possibly for a component related to rigidity, it may be hypothesized that this drug has a more selective action on the cell groups concerned with the function of muscle tone than with cell groups which, when involved, result in tremor. This might mean that a greater degree of stimulation is necessary to influence the function of the latter cells than that of the former. Such a degree of stimulation amphetamine sulfate fails to accomplish. On the other hand, both rigidity and tremor are affected by scopolamine, effects which suggest that this drug influences cell groups having more than one function. If amphetamine sulfate relieves rigidity by a stimulating action on certain cell groups of the basal ganglia, it may be hypothesized that scopolamine influences rigidity and tremor by a depressant action on cortical neurons which are finally concerned with the production of these symptoms. On the other hand, any influence which stimulates the involved cortical neurons might exaggerate tremor and rigidity. Such a stimulus might be emotional or chemical, such as an experimental dose of epinephrine. Since scopolamine prevents the adverse effects of epinephrine, these two drugs may be considered to act on the same area of the cortex.

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That a functional relation exists between the basal ganglia and the frontal cortex is strongly suggested by the physiologic experiments of Rioch and Brenner [4]; Dusser de Barenne and McCulloch,[5] and Mettler, Ades, Lipman and Culler.[6] This relation is further suggested by the improvement in parkinsonian symptoms reported by Klemme [7] after the removal of frontal cortical areas. The symptoms of rigidity and tremor may thus be interpreted as a functional dysbalance between the basal ganglion and the cortex. In this sense, the basal ganglia would normally have an inhibiting influence on the cortex as far as certain components of muscle function are concerned.

The irregular therapeutic results obtained in Parkinson's syndrome are probably best explained by the different degrees of dysbalance between the cortex and the basal ganglia, resulting in cortical activity too great to be influenced by drugs.

SUMMARY AND CONCLUSIONS

A large number of drugs which are usually classified as sympathomimetic, parasympathomimetic or central stimulants were administered to several patients with Parkinson's syndrome. Two of these patients were intensively studied over a period of several months.

1. The drug which most consistently and favorably influences tremor and rigidity is scopolamine, especially when given parenterally. Although both atropine and scopolamine have similar peripheral autonomic effects, the influence of the latter drug on the symptoms of Parkinson's syndrome is much greater because of its relatively stronger sedative action.

2. The drug of next importance in controlling rigidity, but having little or no effect on tremor, is amphetamine sulfate. On the other hand, epinephrine markedly increases both tremor and rigidity, probably by a stimulating action on the cortex, thus contributing to the imbalance present in Parkinson's syndrome. That the effect of epinephrine is central rather than peripheral was demonstrated by its intra-arterial administration, so that its action is confined to the muscles. Its adverse effects on tremor and rigidity are prevented by scopolamine.

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Other so-called sympathomimetic drugs, such as paredrine, propadrine, ephedrine, p-methoxyamphetamine hydrochloride and 3,4-methylenedioxyamphetamine hydrochloride, had slight or no effect on the symptoms of Parkinson's syndrome.

3. Of the drugs usually classified as parasympathomimetic, only acetylcholine and doryl had any favorable influence, and these in small measure. That the effect of acetylcholine is central was shown by the fact that when it was given intra-arterially in such doses as to be limited to peripheral activity it had no effect on either tremor or rigidity. Acetyl-betamethylcholine hydrochloride had little or no effect, and the same was true of furfuryltrimethylammonium iodide. On the other hand, prostigmine methylsulfate increased the rigidity, and its related drug, physostigmine, had no effect.

4. The central stimulating drugs, other than amphetamine sulfate, such as caffeine, coramine, metrazol, theophylline with ethylenediamine and strychnine, had slight or no effect on either rigidity or tremor.

The following general hypothesis is offered to explain the action of certain of the centrally acting drugs. Although the pathologic process of Parkinson's syndrome resides mainly in the basal ganglia, the rigidity and tremor are finally the expression of a functional dysbalance between these structures and the cortex, the latter becoming relatively overactive. Scopolamine may be assumed to produce its favorable results by depressing the cortex, while amphetamine sulfate decreases rigidity by stimulating the basal ganglia.

The clinical administration of both these drugs is probably at present the best pharmacologic method of treating the symptoms of Parkinson's syndrome. Amphetamine sulfate, in our experience, is best given dissolved in gelatin, its effects thus being prolonged.

Administration of these drugs by mouth fails to produce comparable beneficial results in the treatment of Parkinson's syndrome.

DISCUSSION

DR. D. I. SIMONS, New York: Have you found drugs which have an effect on the weakness of which the patients with Parkinson's syndrome complain, or on the festination?

DR. JULIUS LOMAN, New York: The only drug that I know of is amphetamine, which makes patients feel generally better. Amphetamine apparently has two effects: First, it produces a sense of well-being, so that the patients feel subjectively better, and then it has an objective effect on rigidity. In the small doses in which it is usually given clinically, one should not expect much effect on the rigidity. In order to influence the rigidity objectively, at least 20 mg. has to be administered in a dose. No drug, in my experience, influences the festination.

MULTIPLE SCLEROSIS IN THE AMERICAN NEGRO

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Recently Steiner [1] stated that a special study of multiple sclerosis as it occurs in the Negro race was desirable. Although this disease is known to occur in the Negro in the United States, it is regarded as affecting this race less frequently than the native and foreign-born white population. Bailey [2] found that multiple sclerosis accounted for only 3.5 per cent of cases of organic disease of the nervous system among the Negro draftees during the first World War, as compared with the 7.4 per cent obtained for the whole group of draftees. No one has presented figures on the actual incidence or prevalence of multiple sclerosis in a Negro population as compared with that in a white population living under similar circumstances. Indeed, no rates have been given for the race, nor has any attempt been made to analyze the clinical picture of the disease as it appears in the Negro.

The neurologic outpatient department of the Johns Hopkins Hospital is admirably suited to such a study. The hospital is situated in the center of one of the poorer residential districts of the city, and the proportion of Negroes to white persons in the immediately surrounding Eastern Health District of 108,000 persons amounts to 1 in 4, while the percentage of Negroes in Baltimore city was 17.7 per cent in 1930. It is habitual for the Negroes of the area to come to the hospital for care, and most of the patients with neurologic disorders eventually reach this clinic. Those that may attend the other hospitals in the area often fall under the care of members of the staff of the subdepartment of neurology.

The histories of patients with the disease who were seen in the dispensary from Jan. 1, 1929 to Dec. 30, 1939 have recently been carefully analyzed. During this period the diagnostic criteria have been uniform, as the staff of the clinic has remained constant. The records of the Baltimore City Hospitals and the Sinai Hospital were also examined, but it was found that most persons seen in these institutions

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1. Steiner, G.: Multiple Sclerosis: The Etiological Significance of the Regional and Occupational Incidence, J. Nerv. & Ment. Dis. **88**:42, 1938.

2. Bailey, P.: Incidence of Multiple Sclerosis in U. S. Troops, Arch. Neurol. & Psychiat. **7**:582 (May) 1922.

had been patients at the neurologic clinic at one time or another. It was decided to consider as definite cases of multiple sclerosis only those in which a predominant number of the following criteria were satisfied: onset of symptoms between the ages of 15 and 55, a history of remissions and exacerbations of the disease, subjective or objective sensory disturbances, objective evidence of disease of the pyramidal tract or cerebellum, nystagmus, slurred speech, loss of the abdominal reflexes, retrobulbar neuritis, presence of central scotomas, pallor of the optic disks and changes in the cerebrospinal fluid.

Cases were rejected if they failed to fulfil the above mentioned requirements, the Wassermann reaction was positive or another diagnosis was established through subsequent observations. Of the 241 cases collected during this period, 42 were rejected and 199 were retained as definite instances of multiple sclerosis. Including the 30

TABLE 1.—*Relative Incidence of Multiple Sclerosis for the Period 1929-1939 in the Native and the Foreign-Born White Population and in the Negro Population of Baltimore*

Census Figures for Baltimore in 1930	Population	Percentage of Population	Number of Cases of Multiple Sclerosis	Percentage of Cases of Multiple Sclerosis
Native-born white persons	587,714	73.0	107	74.8
Negroes	142,106	17.7	24	16.7
Foreign-born white persons	74,410	9.3	12	8.5
Totals	804,230	100.0	143	100.0

patients seen at the Sinai Hospital and the 17 patients at the Baltimore City Hospitals, 143 of the number were residents of Baltimore, 24 of whom were Negroes. In the total group of 246 patients from all sources, 32 were Negroes. The number and percentage of patients with multiple sclerosis in the native-born white, Negro and foreign-born white populations are shown in relation to the number and percentage of each group in the general population of the city (table 1).

The disease is as frequent among the Negro as among either the native or the foreign-born white population. The rate for the disease over an eleven year period is 17.7 per hundred thousand of the general population and 16.8 per hundred thousand of the Negro group. These figures compare closely with rates computed for the smaller Eastern Health District, containing 108,000 persons, of whom 25 per cent were Negroes. Here there were 4 Negroes in a group of 17, making the rate 14.8 per hundred thousand for the Negroes and 16.4 per hundred thousand for the white persons.

The disease was seen with equal frequency in Negroes of either sex. There were 12 males and 12 females in the Baltimore city group.

Fourteen of the group of 30 Negro patients seen at the Johns Hopkins Hospital had their first symptoms between the ages of 21 and 40, while 9 others noticed their first difficulty between the ages of 15 and 20 years. In none did the onset occur after the fiftieth year. Eleven of the group were engaged in various types of domestic work, including their personal housework; 3 were laborers and 2 operatives, and the rest stated that they were unemployed.

It was possible to separate the patients according to their predominant neurologic disturbance. Thus, 14 patients suffered most obviously from spastic paraplegia; 7 were disabled by cerebellar ataxia, and 4 had complaints predominantly related to visual disorders. This grouping does not necessarily mean that each patient showed only the particular defect

TABLE 2.—*Original Symptoms and Signs of Multiple Sclerosis in Thirty Negroes*

First Symptoms		Signs When First Examined	
Weakness or stiffness of legs	7	Spastic paraplegia	14
Weakness, single extremity	5	Ataxic paraplegia	7
Unsteadiness of legs	4	Bilateral central scotoma	4
Bilateral blurring of vision	3	Monoplegia	2
Unsteadiness and blurring of vision	2	Unilateral central scotoma	1
Unilateral blurring of vision	1	Hemiparesis	1
Hemiparesis (transient)	1	Quadriplegia	1
Weakness of back and blurring of vision	1		30
Paresthesias, arm and leg	1		
Paresthesias, arm and both legs	1		
Paresthesia, both legs	1		
Dysphagia	1		
Tinnitus	1		
Confusional state	1		
	30		

mentioned, but the outspoken feature of their disorder formed the basis of the classification. A patient with spastic paraplegia may also have had ataxia of the arms and signs indicative of retrobulbar neuritis but have been classified as paraplegic.

The original symptoms and the signs in the Negro patients at the time of the first examination are tabulated in table 2.

The abstracts of cases to follow illustrate the clinical history, features and course of the disease as it occurs in Negroes.

CASE 1.—*Progressive spastic paraplegia.*

M. A., a 29 year old Negress, complained of pain in the back and difficulty in walking of two months' duration. The family were in good health, and the patient's past health had been excellent. Six years previously, while running to catch a street car, she found that her legs were weak, clumsy and stiff. She was never able to run afterward. The stiffness and weakness of the legs have been variable, the right leg being the most affected. Two months before coming to the hospital pain developed in the small of her back, together with greater difficulty in walking.

She noted dizziness at this time. Frequency of urination with nocturia had been observed since the onset, and this was intensified in the last six weeks.

Her general physical condition was excellent. The neurologic examination showed temporal pallor of the optic disks. There was horizontal nystagmus when the patient was in the lateral position. Tremors were seen around the eyes and mouth. There was ataxia of the left arm in the finger to nose test, but no abnormality of tone was noted in the arms. The legs were spastic in extension, and voluntary movement and strength were reduced in all movements of these limbs. The patient could walk only with support, having a scissors-like, spastic gait. All forms of sensation were intact. The tendon jerks were overactive in both arms and legs. There were no abdominal reflexes. Ankle clonus and the Hoffmann and Babinski responses were present bilaterally.

The Wassermann reactions of the blood and the cerebrospinal fluid were negative. The spinal fluid was colorless and under average pressure; it contained 2 cells per cubic millimeter and 50 mg. of protein per hundred cubic centimeters and gave a negative Pandy reaction and a colloidal mastic curve of 5555433100. The patient was given quinine sulfate for ten months, without any improvement. The frequency of urination was treated with atropine, with some success. When she was seen again, four years later, her condition was not changed.

CASE 2.—*Retrobulbar neuritis; repeated remissions, and a defect predominantly cerebellar in character.*

R. S., a 30 year old Negress, complained of weakness of the legs and staggering. There was no family history of nervous or mental disease. The past history contributed little of significance.

Seven years prior to her visit to the hospital she suddenly lost her vision. The blindness persisted for five days; then vision gradually returned. She found she staggered when she walked. Two weeks after the spell of blindness she became unconscious for a half-hour.

The patient was admitted to the hospital after a "stroke," which involved the right leg but prevented her from walking for only three days. Again, three years later, she was unable to move her right leg for a short period. This trouble recurred three months later, though function returned in two weeks. She had a "pins and needles" sensation in this leg from the knee down. Both legs were constantly cold. She complained of frequency of micturition, with nocturia.

On examination she appeared well developed but poorly nourished. The functions of the cranial nerves were normal. There was decreased tone of both arms and legs, more marked in the latter. An intention tremor was brought out by the finger to nose test. Ataxia and incoordination of the legs were manifest in performing the heel to knee test. Her station was unsteady, and the gait showed gross ataxia of the cerebellar type. There was slight hyperesthesia over the feet, with failure to appreciate vibration over the tibial malleoli. The other forms of sensation were perceived normally. The tendon reflexes were equal and active on the two sides. The ankle jerk was overactive on both sides. There was no clonus, but both plantar responses were extensor. The abdominal reflexes were absent.

The Wassermann reactions of the blood and the spinal fluid were negative. The spinal fluid was clear and under normal pressure; it contained 2 mononuclear cells per cubic millimeter and 25 mg. of protein per hundred cubic centimeters and gave a flat colloidal mastic curve and a negative Pandy reaction. The patient was treated for three months with quinine, without improvement. After one month of therapy nystagmus and head tremor were apparent.

CASE 3.—*Bilateral hemiparesis, more marked on one side.*

G. H., a Negro aged 40, had been unable to flex his right leg as well as formerly for four months before coming to the hospital. The weakness progressed, and for six weeks his gait had been impeded.

His general physical status was good. Neurologic study revealed rotatory nystagmus. There was tremor of the tongue. The cranial nerves otherwise functioned well. Both arms were weak, the left more than the right. Spasticity was marked in the right leg and less in the left. Strength in all movements was greater in the left leg than in the right. The gait showed spasticity in movement, with a tendency to circumduction at the thighs. There were no sensory defects. The tendon reflexes were overactive in both arms and legs. There was finger, wrist and ankle clonus on the right; Hoffmann and Babinski responses were present on both sides.

The Wassermann reactions of the blood and the spinal fluid were negative. The spinal fluid was clear, colorless and under normal pressure. There was no block. There were 8 cells per cubic millimeter, 50 mg. of protein per hundred cubic centimeters and a flat colloidal mastic curve. The Pandy reaction was negative. There was no improvement on quinine therapy for five months. The patient was then transferred to the Baltimore City Hospitals for further care.

CASE 4.—*Recurrent attacks of retrobulbar neuritis; gradual development of sensorimotor defects.*

T. S., a 35 year old Negro, was referred from the department of ophthalmology to the syphilis clinic because of early bilateral atrophy of the optic nerve. He himself complained of nearsightedness. There was no history of familial disease or chronic illness among his relatives. His past health had been good except for the childhood exanthems and fracture of his right arm at the age of 33. There was a history of gonorrhea at the ages of 21 and 26, but he never had a chancre or a positive reaction of the blood for syphilis. There was 1 child by his first wife and 2 by the second, all of whom were healthy. There had been no miscarriages.

At the age of 24 he was examined for the army and was found unable to read type with the right eye. Six years later he suddenly noticed that he was unable to read the time from the face of his watch or see the opposite side of the street. He was treated for some months, and his vision improved. Three years later he was referred to the ophthalmologic clinic, where he was found to have early atrophy of the optic nerve. Neurologic examination showed early optic atrophy, overactive knee jerks and "suspicious" extensor plantar responses. The diagnosis of multiple sclerosis was thought probable. The Wassermann reactions of the blood and the spinal fluid were negative; the fluid was clear, under normal pressure and contained no cells, but the mastic curve was reported as 5532100000.

In spite of the negative serologic reactions, he was given ten months of antisyphilitic therapy. Then it was observed that the abdominal reflexes were no longer present and the mastic curve of the spinal fluid had become normal. Four years later he was seen again, complaining of impotence of six months' duration. The neurologic signs were unchanged, except that he was not able to discriminate compass points in the hands. Within a year he returned with complaints of weakness, easy fatigability and stumbling when he walked. There was urinary incontinence, but impotence was his chief complaint. He had auditory hallucinations and thought that some one was putting a spell on him. At this time he had a definite bilateral extensor plantar response.

Six months later a complete neurologic study was made. There was a central scotoma on the right, and visual acuity remained at 20/200 bilaterally. The optic disks were white and sharply outlined. There was horizontal nystagmus, more marked on looking to the right. The legs were spastic, and the gait was impeded. All the tendon reflexes were overactive. Babinski responses were obtained, and the abdominal and cremasteric reflexes were not present. There was no further progression of the disease during the next two years.

CASE 5.—*Rapidly developing intellectual deficit, which was thought to be due to a tumor of the midbrain or to hemorrhage.* (The case report and pathologic material are presented by permission of Dr. George H. Patterson and Dr. Kenneth Abbott, of Los Angeles.)

E. M., a 52 year old Negress, was brought to the hospital because of sudden loss of consciousness. The family and past histories contributed little to the understanding of her illness. For the five years previous to her entry she had "poor muscle control" and had been unable to walk because of unsteadiness. Incontinence and failing memory had been observed for the last ten days. She suddenly became unconscious on the day of admission.

Occipital cortex (case 5), showing demyelinated plaques in the subcortical white matter. Spielmeyer preparation; × 4.

The patient was comatose, with the eyes deviated to the right. The temperature was 98 F., the pulse rate 110, the respiratory rate 16 and the blood pressure 140 systolic and 70 diastolic. There were a few moist rales at the bases of the lungs. The lower extremities appeared atrophic. Tendon reflexes in the extremities were overactive, with a bilateral Babinski response.

The spinal fluid was clear and under a pressure of 115 mm. of water; it contained 3 lymphocytes per cubic millimeter and had a colloidal benzoin reaction of 3333300000. The Wassermann reactions of the blood and the spinal fluid were negative. The urine was clear. Ventriculographic examination showed no abnormalities.

The comatose state persisted, and the patient finally died, with respiratory failure. Autopsy showed definite thickening of the leptomeninges over the dorsolateral surface of the frontal lobes, most marked along the superior longitudinal sinus, with some associated atrophy of the convolutions in this area.

After hardening, sagittal sections were made of the brain. These showed extensive, grayish, shiny plaques in the white matter, particularly in the centrum ovale, the corpus callosum, the optic radiation and the periventricular areas. Plaques were also seen in the pons, cerebellum and medulla.

On microscopic study large scarred areas were seen in which the nerve tissue had been replaced by astrocytes, the fibrils of which were arranged in parallel bundles. At the margin of these areas there was some condensation of oligodendroglia. Sections stained for myelin sheaths showed large, sharply outlined areas in which the myelin was lost and all the intervening axis-cylinders were gone.

COMMENT

The foregoing statistics and clinical presentations make it clear that multiple sclerosis occurs as frequently and in the same form in the Negro as in the white population in Baltimore. The opinion expressed by Brickner [3] that the disease is uncommon in the Negro and Steiner's [1] failure to find any cases among Negroes in New Orleans would appear, in the light of the experience in this clinic, to be due to the nature of the practice in which these authors were engaged. Brickner based his statement on his experience in a neurologic practice in New York city, where the percentage of Negroes in the general population was 4.7 in 1930.[4] It is to be doubted that many Negroes consulted him, owing to their relatively small number and their poor economic status. Steiner spent six months in New Orleans and found multiple sclerosis only among foreign-born persons. The nature of his practice (whether general or neurologic) and the possibilities of extensive consultation were not stated. Davenport [5] also stated that Negroes are "probably less subject to the disease than the white race." Bailey's figures for the relative frequency of the disease as compared with that of other disorders of the nervous system have been mentioned. However, the susceptibility of the various races is not likely to be determined by comparing the percentage frequency of multiple sclerosis with that of other diseases of the nervous system in those races. The best method would be to obtain rates for each race in large population groups. This is the method used here.

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3. Brickner, R. M., and Brill, N. Q.: Dietetic and Related Studies in Multiple Sclerosis, Tr. Am. Neurol. A. **66**:157, 1940.

4. Fifteenth Census of the United States, 1930: Abstract of Fifteenth Census of the United States, United States Department of Commerce, Bureau of the Census, 1933.

5. Davenport, C. B.: Multiple Sclerosis from the Standpoint of Geographic Distribution and Race, Arch. Neurol. & Psychiat. **8**:51 (July) 1922.

Criticism may be directed against the statement that multiple sclerosis is rare in other countries or races. The reports of Miura,[6] Sprawson[7] and Verhaart,[8] which suggest the infrequent occurrence of multiple sclerosis in Japan, China, India, Africa and the Netherland East Indies, are again based on opinions rather than on careful studies of the disease in large population groups. No figures have been presented for these countries or for their racial populations.

In reviewing those studies which do present rates found in large population groups it is evident that even such figures are not comparable. No clear distinction has been drawn between the incidence rate, which represents the number of new cases per unit of population in a given period, and the prevalence rate, which represents the number of cases per unit of population present in a given period. Love and Davenport's[9] figure of 10.4 per hundred thousand of the population for the United States was obtained from examinations of the draftees during the first World War. This may be said to be a prevalence rate for one and a half years but can be criticized, as the study included only a select group of young men. The figure given by Allison[10] is a prevalence rate for one year in North Wales. The rate of 11.7 compares closely with that of Love and Davenport. The rate which I have shown in table 1 for an eleven year period and which Bing and Reese[11] gave for Switzerland for a five year period are combined incidence and prevalence rates, as they include cases in which multiple sclerosis was present at the beginning of the investigation and those in which the disease developed during the period of study. In another paper[12] a discussion of these rates is given further consideration. Until more adequate data are available, it is preferable to reserve judgment concerning the susceptibility to multiple sclerosis of various races or of persons living under different geographic conditions.

The prevalence rate for the Eastern Health District of Baltimore in a given month equaled 13 per hundred thousand. This makes it clear that the opinion of a single practitioner is likely to be valueless, particularly if he is not constantly engaged in neurologic practice, since most

6. Miura, K.: Deutsche Ztschr. f. Nervenh. **41**:146, 1911.

7. Sprawson, C.: Disseminated Sclerosis Among Indians in India, Far East A. Trop. Med., Tr. Seventh Cong. (1927) **1**:8, 1928.

8. Verhaart, W. J. C.: Ophthalmo-Neuromyelitis, multiple und diffuse Sklerose bei Ost-Asiaten in Niederl. Ost-Indien, Acta psychiat. et neurol. **13**:93, 1938.

9. Love, A. C., and Davenport, C. B.: Defects Found in Drafted Men, Washington, D. C., Government Printing Office, 1920.

10. Allison, R. S.: Disseminated Sclerosis in North Wales, Brain **53**:391, 1930.

11. Bing, R., and Reese, H.: Die multiple Sklerose in der Nordwetschweiz, Schweiz. med. Wchnschr. **56**:30, 1926.

12. Kolb, L. C.; Langworthy, O. R., and Cakrtova, M.: The Multiple Sclerosis Problem in Baltimore City, Am. J. Hyg. **35**:1, 1942.

physicians in this country care for an average of 500 to 1,000 persons. In the neurologic dispensary of the Johns Hopkins Hospital, which receives, aside from the local patients, many visitors from other states, not more than 2 new patients with multiple sclerosis are seen each month.

It is impossible to state whether the character and frequency of the disease in the American Negro differ from those in Negroes in their native habitat. There are no adequate comparative studies from Africa. Climatic differences and the admixture of Negro and white blood which occur in this country might be expected to produce some modifications provided racial and climatic factors were known definitely to have some effect on the character and course of the disease.

The fourth case illustrates another problem in the diagnosis of multiple sclerosis in the Negro. In Baltimore the frequency of syphilis in the Negro is such that neurologic disorders are immediately suspected as being syphilitic in origin. Thus in many of the cases of multiple sclerosis in Negroes treatment for syphilis has been instituted in spite of both negative reactions of the blood and spinal fluid and clinical findings consistent with the diagnosis of multiple sclerosis. With the great frequency of syphilis in the American Negro it is not unlikely that some will have both syphilis and multiple sclerosis. Several Negroes have been seen who would seem to fall into this group. The clinical findings suggested multiple sclerosis; the Wassermann reaction of the blood was positive, but antisyphilitic treatment failed to relieve or prevent the progress of the disease.

SUMMARY

Negroes in Baltimore are as subject to multiple sclerosis as the native and the foreign-born white population. The clinical features of the disease in the Negro are similar to those seen in the white man. The disease in the Negro is often mistaken for syphilis and in some instances may occur with syphilis in the same person.

THE HUMAN PYRAMIDAL TRACT

V. POSTNATAL CHANGES IN THE AXONS OF THE PYRAMIDS

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The postnatal changes in the performance of the striated muscles of man must depend on concomitant alterations in the efferent structures of the nervous system and muscles. The pyramidal tract, because of its isolation and accessibility in the pyramids, offers an opportunity to compare the development of somatic motor neurons and function subsequent to birth.

It is well known that during most of the first year of infancy movements are involuntary and nonpurposeful. In man the ability to perform or initiate voluntary muscular action (kinetism) commences late in the first year and requires some time for integration. Maximum muscular efficiency is acquired probably toward the end of the second or the first part of the third decade. In senility there is loss in the speed, flexibility and coordination of movement, conditions frequently accompanied by tremor.

Instances of injury to the central nervous system during birth are common, and autopsy statistics indicate that diffuse and serious damage occurs in the majority of such cases. Involvement of motor paths at this time apparently produces less motor deficit than in adult life, and certain neurologic symptoms (spasticity) may remain latent or masked for months. The process of myelination, which occurs late in the somatic motor tracts, has been suggested as a cause of this difference in effect in the infant and in the adult.[1] According to this view, lesions affecting the motor system after the efferent tracts have become myelinated and presumably functional cause more impairment. This implies that the myelin sheath is more important than other parts of the neuron. It does not account for the fact that the pyramidal tract contains many unmyelinated fibers. It seems to me that the growth of the nerve cell, with its branches, collaterals and terminal connections, should be of paramount significance in integration of nerve function.

From the Department of Anatomy of the Medical College of the State of South Carolina.

1. Kennard, M. A.: Relation of Age to Motor Impairment in Man and in Subhuman Primates, Arch. Neurol. & Psychiat. **44**:377-397 (Aug.) 1940. Ford, F. R.: Cerebral Birth Injuries and Their Results, Medicine **5**:121-194, 1926.

The role assigned to the myelin sheath by the majority of neurologists is the auxiliary one of insulation.

In attempting to explain the cause of the cerebral birth palsies, clinicians and pathologists have focused their attention on the fibers of the pyramidal tract.[2] Scarcity, fineness, incomplete myelination, imperfect development and atrophy of the fibers of the pyramidal tract have been mentioned as possible causes of spastic diplegia or paraplegia. A knowledge of the normal appearance of these fibers at various ages may be of value in studying the neuropathology of motor diseases.

MATERIAL AND METHODS

Medullas were obtained at autopsy from twenty minutes to twelve hours post mortem from persons aged 1, 3, 8 and 11 months and 2, 22 and 80 years and from a newborn infant. The causes of death were diarrhea, pneumonia, peritonitis and accident. The specimens were hardened in Davenport's fixative, and 5 micron sections taken just above the pyramidal decussation were stained by the protargol (protein silver) technic. A general study of the pyramids was made at a magnification of 1,125, and photomicrographs, presented in the accompanying figure, were taken at a magnification of 720.

RESULTS

The areas, expressed in square millimeters, of the pyramidal tract at a level just above the motor decussation for the eight ages represented were as follows: newborn infant, 1.89; 1 month, 2.75; 3 months, 2.18; 8 months, 2.98; 11 months, 5.43; 2 years, 5.83; 22 years, 11.71, and 80 years, 7.25 (shrinkage computed). Between birth and maturity the pathway increases in area about six times. In this series there was approximately a doubling in area between the ages of 8 and 11 months and again between the ages of 2 and 22 years. The area of the pyramidal tract of the 80 year old subject was 62 per cent of that of the 22 year old subject.

Throughout life changes occur in the caliber of the axons of the pyramidal tract (figure). During the first eight months of life the fibers are uniformly small, closely packed together and less responsive to the stain used. This interval appears to be a quiescent period, with little increase in the area or in the magnitude of fibers. At 11 months of age a few predestined axons begin to grow more rapidly than others. At 2 years the fibers resemble those of the adult. There is definite differentiation into small, medium and large axons, but the largest are only about one-fourth to one-third the size of similar mature fibers. The characteristic picture of the adult pyramid shows a few large, more medium and many small axons.

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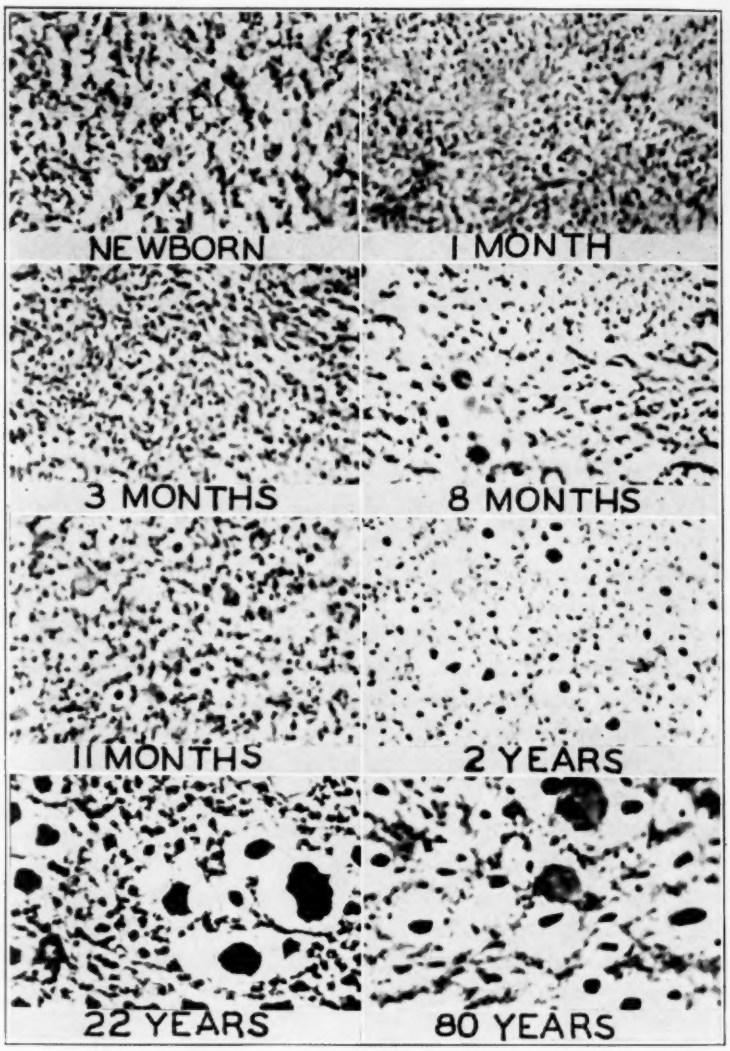
2. (*a*) Collier, J.: The Pathogenesis of Cerebral Diplegia, Brain **47**:1-21, 1924. (*b*) Rhein, J. H. W.: Cerebral Palsies Without Demonstrable Anatomical Findings, J. Nerv. & Ment. Dis. **40**:639-650, 1913.

When the specimen from the 80 year old subject was compared with that from the 22 year old subject the area and axons of the tract in the former were found to be smaller. This may represent a marked indi-



Unretouched photomicrographs of the human pyramidal tract from sections at a level just above the motor decussation, showing axons at various ages of postnatal life. The two spherical masses at the upper center of the specimen from the 80 year old subject represent corpora amylacea. Protargol (protein silver) stain; × 720.

vidual variation or an actual senile change. Some fibers were missing, and a few appeared to be in various stages of breakdown. Another

feature of the section from the old subject was the presence of many corpora amylacea. A count of 1,165 was made in the pyramid of one side in a 5 micron section.

Computations, at the level studied, indicate that all the fibers of the pyramidal tract are present at birth. Although the area of the pyramidal tract of the 22 year old subject was about six times that of the newborn, the latter had about six times the number of fibers per unit area, as determined by average counts with a Whipple square. When the area increased, the number of fibers per square millimeter decreased. Thus, the total number of fibers remained fairly constant, except in the 80 year old subject, who had only about two thirds as many as did the 22 year old subject. This is due principally to the smaller square area.

COMMENT

On the basis of a silver impregnation study, the pyramidal tract is concluded to be of a different anatomic character in infancy, in maturity and in old age. Early in postnatal life all the axons are apparently present; they are small, of uniform size, closely packed together and possibly of a different chemical nature than when mature. If the pyramidal tract is concerned with either voluntary innervation or skilled digital movements, it may be safe to add that this histologic picture is associated with nonfunction. There is evidence of a change occurring during the eighth or eleventh postnatal month (figure). At this time there is acceleration in growth of a few predestined axons, during the interval when the process of myelination is active, which phenomenon has been correlated with function.[1] Duncan [3] found that the larger fibers in the nervous system myelinate earlier than the smaller ones. The fibers of the pyramidal tract which are destined to become large may thus myelinate first. The postnatal development of the pyramidal tract, therefore, may occur as a unit, with the following events occurring synchronously: increase in the length and diameter of the axons, change in chemical nature, myelination and integration of function. There is a possibility that some of the axons increase in diameter more than others in order to increase their velocity of conduction. The nerve fibers must increase in length in proportion to the growth of the brain stem and cord, and since speed and dexterity of movement improve with age in early childhood, there is a need for greater velocity of conduction. Collier [2a] stated that in the majority of cases of cerebral birth palsies the clinical and pathologic evidence indicates involvement of the pyramidal system. A feature of the pyramidal tract in infancy, which may

3. Duncan, D. D.: A Relation Between Axone Diameter and Myelination Determined by Measurement of Myelinated Spinal Root Fibers, J. Comp. Neurol. **60**:437-472, 1934.

be of pathologic significance, is the crowding of minute and delicate fibers into a small area, where they are vulnerable to even small lesions.

The early anatomic picture of the pyramids is not incompatible with those reported for the infant cortex. Conel [4] has shown that in the infant the so-called Betz cells are rounder and smaller and the Nissl substance is less differentiated than in the adult and that these cells cannot be distinguished from the large round cells of the fifth layer of area 6. He reported [5] that very little change occurs in the cortical cells during the first month of postnatal life. The axons below in the pyramids are likewise more uniform and undergo no augmentation in size at this period.

The morphologic character of the mature pyramidal axons has been discussed more fully elsewhere.[6] Numerically, the minute axons are predominant and those of large caliber relatively scarce, although they make a good appearance by reason of their magnitude. Foerster,[7] on the basis of electrical stimulation of the cortex, has called the pyramidal tract a "fast train system," but certainly only relatively few axons are designed for speedy transmission of impulses. Lloyd [8] has reported both slow and fast conducting fibers in the pyramidal tract of the cat, which is what I should expect on the basis of its anatomy.

In the 80 year old subject the area and axons of the pyramidal tract were of smaller size. How much of this may be due to individual variation and how much to senility is difficult to say without studying a larger series. By calculation, the tract of this subject had only about two thirds as many fibers as that of the 22 year old specimen. A few of the fibers were in various stages of degeneration, and some had totally disappeared. Andrew and Cardwell [9] have reported neuronophagia, satellitosis and loss of Nissl substance in older persons. Gardner [10] found considerable reduction in the number of myelinated fibers in the dorsal roots in persons between 70 and 79 years of age.

4. Conel, J. L.: The Cortex of the Newborn, in the Postnatal Development of the Human Cerebral Cortex, Cambridge, Mass., Harvard University Press, 1939, vol. 1.

5. Conel, J. L.: Development of the Human Cerebral Cortex During the First Month of Life, Arch. Neurol. & Psychiat. **45**:387-388 (Feb.) 1941.

6. Lassek, A. M., and Rasmussen, G. L.: The Human Pyramidal Tract: A Fiber and Numerical Analysis, Arch. Neurol. & Psychiat. **42**:872-876 (Nov.) 1939.

7. Foerster, O.: The Cerebral Cortex in Man, Lancet **2**:309-312, 1931.

8. Lloyd, D. P. C.: The Influence of Pyramidal Excitation on the Spinal Cord of the Cat, Am. J. Physiol. **133**:P175-P176, 1941.

9. Andrew, W., and Cardwell, E. S., Jr.: Neuronophagia in the Human Cerebral Cortex in Senility and in Pathologic Conditions, Arch. Path. **29**:400-414 (March) 1940.

10. Gardner, E.: Decrease in Human Neurones with Age, Anat. Rec. **77**:529-536, 1940.

In my specimen from the 80 year old subject there must have been a tremendous number of corpora amylacea present in the central nervous system at the time of death, for 1,165 were enumerated in the pyramidal tract of one side in a 5 micron section taken just above the motor decussation. Boyd [11] stated that these hyaline bodies represent microglia cells, or that in some cases they may be formed from the oligodendroglia. If this is true, they indicate degeneration in the supporting elements of the central nervous system, and I should expect concomitant signs of neuronic deterioration.

CONCLUSIONS

The fibers of the pyramidal tract undergo the following postnatal changes: Early in life all the axons are apparently present and are small, delicate, uniform in caliber, crowded and possibly of a different chemical nature than when mature. During this period they may be nonfunctional and vulnerable to small lesions. At 8 months of age, when voluntary movements are attempted, certain fibers commence to expand at a more rapid rate than others. Individual growth continues, until at 2 years of age the pyramidal tract simulates in miniature that of an adult. At 22 years of age the pathway possesses a few large, more medium and many minute axons. In senility, on the basis of observations on 1 specimen, there is a decrease in number and diameter of fibers. It seems reasonable, also, to conclude from the study that integration of the pyramidal tract occurs through morphologic and chemical changes in both the axons and the myelin sheaths rather than in the latter alone and that different physiologic motor states may be explainable, in part at least, on a neuroanatomic basis.

11. Boyd, W.: A Textbook of Pathology, ed. 3, Philadelphia, Lea & Febiger, 1938.

OTITIC THROMBOSIS OF THE CEREBRAL SINUSES AND VEINS SIMULATING MULTIPLE BRAIN TUMORS

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It is generally not appreciated that in venous thrombosis of the brain there may occur a widespread destructive process which may present a most confusing clinical picture. The following case is a good illustration of the difficulties that may be encountered in the clinical diagnosis of thrombosis of the cerebral veins and sinuses.

REPORT OF A CASE

History.—A 46 year old married man was admitted to the Montefiore Hospital on May 24, 1938, complaining of weakness of the left upper extremity of one month's duration. His family history was irrelevant. Except for a painless, intermittently discharging right ear, with slight impairment of hearing for the past three years, he had been well until April 23, 1937. On that day, while at work, he stepped into a bucket of cold water and fell down, striking the back of his head and the lower part of his back against a wooden platform. He sustained no external injuries and did not lose consciousness. After a short rest, he traveled unassisted to his home, a distance of 10 miles (16 kilometers) from his place of employment.

Five days later he returned to his work, and, except for some intermittent discomfort in the back, he was well until two weeks later, when he began to have frequent, urgent and painful urination. This persisted until June 2, 1937, when there appeared frank hematuria. Seven days later he was admitted to the Mount Sinai Hospital, where a left ureteronephrectomy was performed. The pathologic diagnosis was tuberculous pyelonephritis and ureteritis. On the twentieth postoperative day he was discharged "completely asymptomatic." In that hospital, except for evidences of healed bilateral pulmonary tuberculosis and the aforementioned urinary condition, the physical examination, including that of the nervous system, revealed nothing significant.

During the next four months the patient gained 30 pounds (13.6 Kg.) in weight, and on Oct. 25, 1937 he resumed his occupation. On April 25, 1938, while at work, there suddenly appeared a jacksonian seizure, involving the right leg. The seizure lasted a few seconds, after which he attempted to resume his work but was unable to continue because of weakness of the entire left upper extremity and a sensation of numbness and tingling in the hand and fingers of that extremity.

From Dr. Keschner's private service and the Neuropathological Laboratory of the Montefiore Hospital.

The jacksonian seizure did not recur, and during the next few days there was a slight return of power in the affected limb. The patient remained in this condition until May 4, 1938, when he was referred to one of us (Keschner) by an insurance company for an opinion as to the nature of the neurologic condition and its compensability under the Workmen's Compensation Act, in view of the accident which he sustained on April 25, 1937 and which had been adjudicated as compensable.

Examination.—Examination on May 4 disclosed the following changes: Both pupils reacted better in accommodation than to light. The fundi, visual fields and ocular movements were normal. There were slight weakness of the left side of the face of supranuclear type, right middle ear deafness with perforation of the drum and slight mucopurulent discharge; left hemiparesis of upper motor neuron type, more marked in the upper extremity; a Babinski sign on the left; a Hoffmann sign bilaterally; questionable hypalgesia, hypesthesia and hypothermesthesia over the left upper extremity; slight euphoria, and considerable psychomotor retardation.

These findings suggested the presence of a lesion in the right cerebral hemisphere, and, in view of the history of a jacksonian seizure in the right leg, the possibility of another lesion in the left motor area was seriously considered. Because of the history of tuberculosis, the intracranial process was thought most likely to be multiple tuberculoma. Hospitalization and encephalographic study were advised, but because of the patient's unwillingness, admission to the hospital was delayed until May 24, 1938, when he finally entered the Montefiore Hospital.

Examination on admission disclosed nothing other than the changes previously noted. On June 1 the patient was subjected to air studies, injections being made by the lumbar route. Spinal puncture yielded a fluid which was at first slightly hazy and faintly pinkish yellow and was under an initial pressure of 92 mm. of water; it contained numerous red but no white cells. After the removal of 7 cc. of fluid the succeeding fluid was colorless and clear and contained 19 red blood cells per cubic millimeter. The Pandy reaction was negative; the protein content was 46.9 mg. per hundred cubic centimeters, and the Wassermann and colloidal gold reactions were negative. Smears and cultures did not reveal tubercle bacilli, and inoculations of the fluid in guinea pigs gave negative results. The encephalographic studies disclosed that the lateral ventricles were well outlined and symmetrically dilated, without evidence of shift. The third ventricle was well outlined, dilated and median in position. The fourth ventricle was slightly dilated. Cortical atrophy was evidenced by the presence of an increased amount of fluid in the subarachnoid spaces. Except for some calcifications in the falx, roentgenographic examination of the skull disclosed no abnormalities.

Examination of the blood showed 92 per cent hemoglobin, 5,650,000 red cells, 8,100 white cells, with a normal differential count, a negative Wassermann reaction, and a sedimentation rate of 14 mm. at the end of one hour. The chemical constituents of the blood and the results of urinalysis were normal. Roentgen examination of the chest disclosed old, fibroid tuberculosis of the upper lobes of both lungs and a few calcified nodules in the lower lobes, but no evidence of recent disease. Smears of material from the discharging ear disclosed no tubercle bacilli.

Course.—Except for slight generalized headache, which gradually increased in severity, the patient was comfortable until the fifth day after encephalographic examination, when he became nauseated and vomited. He then complained of pains radiating from the head to the back of the neck and both arms. He was afebrile, and the pulse ranged from 76 to 100 per minute. On the sixth day there appeared urinary incontinence, nuchal rigidity, a bilateral Kernig sign, ankle clonus

and a Babinski sign. The temperature rose to 100.4 F. and the pulse rate was 116. Lumbar puncture yielded hazy fluid under a pressure of 400 mm. of water; it contained 12 lymphocytes per cubic millimeter, 67 mg. of sugar, 73.4 mg. of protein and 794 mg. of chlorides per hundred cubic centimeters. Smear and cultures of the spinal fluid were negative for organisms. The Ayala index was 4.5. Ten minutes after spinal puncture the patient had a generalized convulsion, with another two hours later. After the convulsions he became stuporous. On the ninth day after encephalographic examination he had several more convulsions, the temperature rose to 103 F., the pulse rate was 110 to 120, the respiratory rate was 64 and there was a marked increase in the signs of meningeal involvement. He was again subjected to lumbar puncture, which yielded a hazy fluid under a pressure of 460 mm. of water and contained 29 lymphocytes per cubic millimeter; the Pandy reaction was positive; the reaction to the tryptophan test was positive, and there was definite pellicle formation. The stupor deepened, and the convulsions increased in severity and number. The patient died on the ninth day after encephalographic examination.

Necropsy.—General Examination: There were old tuberculosis of the apexes of both lungs, parenchymatous degeneration of the viscera and a healed nephrectomy wound on the left side. Only the middle ears, the dural sinuses and the central nervous system will be described in detail.

Middle Ears: Sections of the ears and their bony parts were decalcified, embedded in pyroxylin and stained with hematoxylin and eosin and by the Giemsa and Van Gieson methods. The various fragments of the right middle and inner ear consisted of necrotic bony material, in some of which the organ of Corti was identified. Part of the bony tissue was separated by loose connective tissue. These fragments were filled with lymphocytes, plasma and endothelial cells, a few polymorphonuclear leukocytes and congested and proliferated blood vessels. Neither giant cells nor tubercles were seen. Tubercle bacilli were not found in specially stained sections.

Dural Sinuses: The superior longitudinal and right sigmoid sinuses contained a thrombus showing slight organization.

Microscopically, sections of the superior longitudinal sinus showed a mural thrombus with beginning organization (fig. 1). The thrombus was filled with hemorrhagic material (fig. 2 *H*) and inflammatory cells, consisting of polymorphonuclear leukocytes and lymphocytes (fig. 2 *I*); some of these were enmeshed in fibrous connective tissue (fig. 2 *OR*). In some areas there were collections of lymphocytes in the wall of the sinus and in the adventitial spaces of the vessels.

A section of the lateral sinus disclosed a similar process. In several places the thrombus was attached to the wall of the sinus by a few strands of connective tissue. Hemosiderin and inflammatory cells were observed in the thrombus.

Brain: Gross study: The dura was congested, cyanotic and tense. The dural sinuses were filled with clots, which were slightly adherent to the walls. The pia-arachnoid was under tension and contained yellowish streaks along the larger cortical vessels. The fissures of the cerebral convolutions appeared partially obliterated. The subarachnoid cortical vessels were congested and distended, most of them being thrombosed. The superficial cortical vessels of the left hemisphere were dilated. In the left parieto-occipital region there was a magenta-colored softening, approximately 3½ by 4 inches (9 by 10 cm.) in diameter. In coronal sections the tip of the anterior horn of the left ventricle appeared slightly

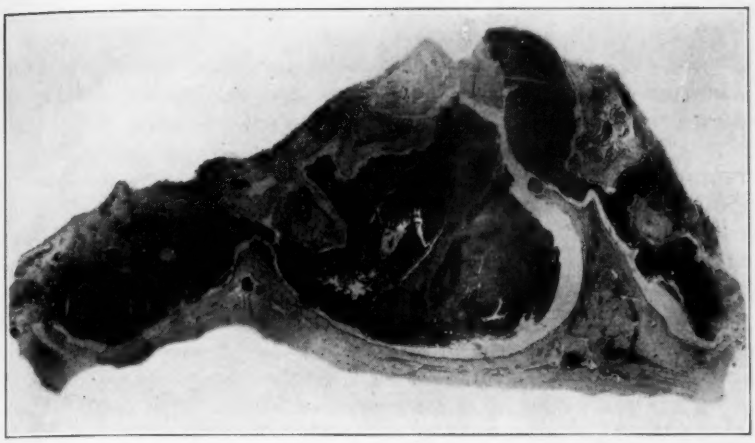

Fig. 1.—Superior longitudinal sinus with a thrombus attached to its inner wall, showing beginning organization.

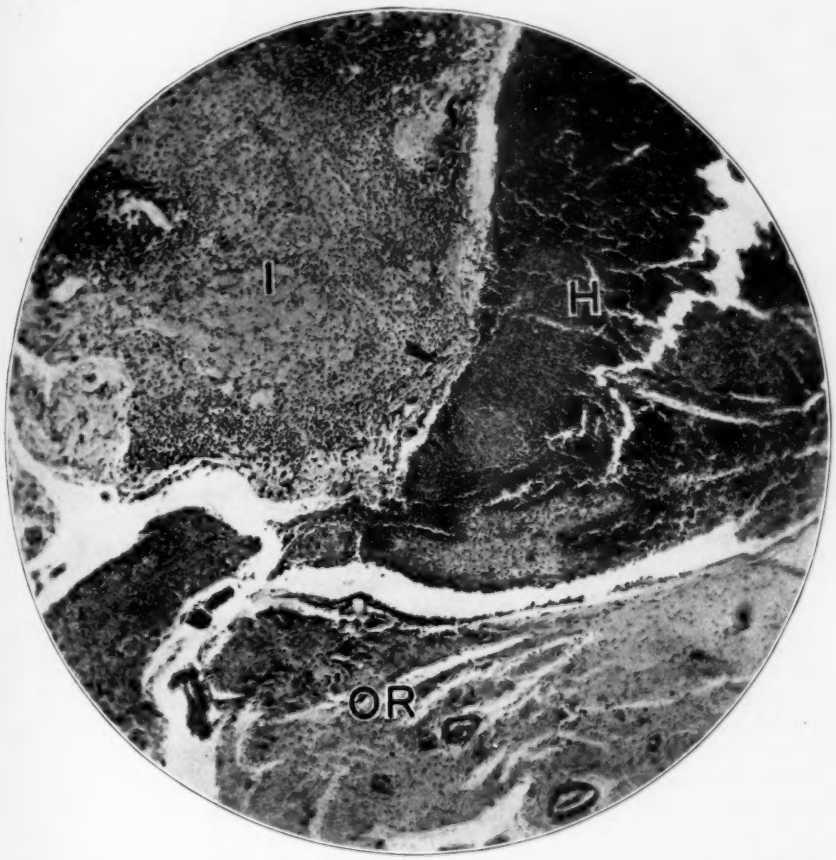

Fig. 2.—Thrombus from the superior longitudinal sinus illustrated in figure 1, showing hemorrhage (*H*), an inflammatory focus (*I*) and a partly organized thrombus (*OR*), consisting of connective tissue and vessels surrounded by inflammatory cells. Hematoxylin-eosin stain; × 30.

constricted. The third ventricle was distorted and shifted to the right (fig. 3). Hemorrhagic areas in the left hemisphere involved the first and second frontal, the premotor, the motor and the parietal convolutions (figs. 3 and 4). Small hemorrhagic areas also involved part of the motor, superior parietal and temporal convolutions on the right side. In sections through the posterior horns large and multiple small hemorrhages were found in the inferior parietal and occipital convolutions on both sides, more so on the left. On the right side there was also a subarachnoid hemorrhage in one of the occipital fissures. A small area of softening was seen in the right gyrus cinguli close to the corpus callosum.

Microscopic Study: Complete coronal sections through the hypothalamus, red nucleus and occipital convolutions and small blocks of the motor, parietal and occipital convolutions and spinal cord were embedded in pyroxylin and stained by

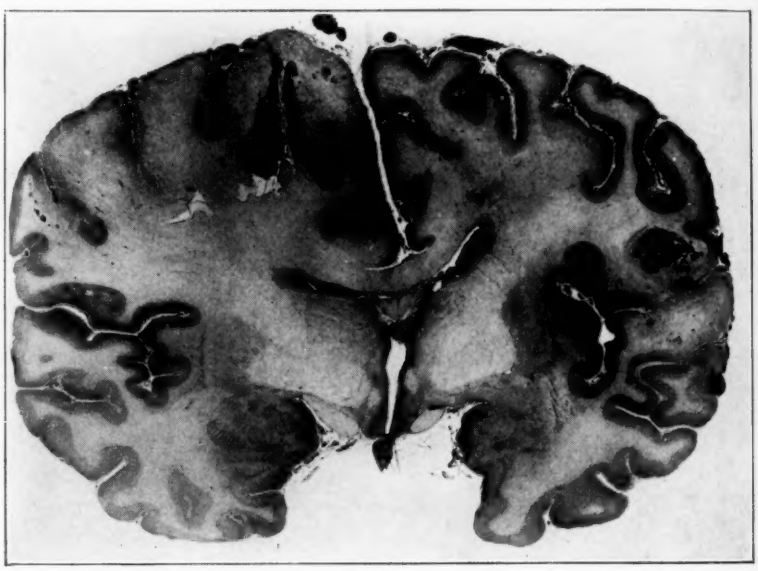

Fig. 3.—Hemorrhages and thromboses of the veins along the distribution of the left, and also partly of the right, middle cerebral vessel. Note the subarachnoid hemorrhages. There is ischemia of the left and right parietal and the right temporal convolutions. Cresyl violet stain.

the myelin sheath and cresyl violet methods. Blocks from the hemorrhagic regions were also embedded in paraffin and stained with hematoxylin and eosin.

In the complete coronal sections through the third ventricle, in addition to the large hemorrhages described on gross examination punctate hemorrhages could be discerned with slightly higher magnifications. The white matter of the left hemisphere was edematous and partially demyelinated. Some of the myelin sheaths and axis-cylinders were destroyed; others showed various pathologic changes, such as swelling or disintegration. In the cresyl violet preparation, the meninges, in places, were slightly proliferated and infiltrated with polymorphonuclear leukocytes, lymphocytes, plasma cells and red blood cells.

A number of the larger hemorrhages had a well defined border and in places were lined by a single layer of endothelial cells. There was distortion in the

arrangement of the cytoarchitectural layers. The various cortical layers were filled with numerous hemorrhages. Most of the red blood cells formed clusters of various sizes, some of which had the appearance of ring hemorrhages. The red blood cells were not swollen, decolorized or shrunken. No hemosiderin was present. There was little or no glial proliferation. In some areas, however, the glia apparatus was destroyed and had a honeycombed appearance. Many cerebral vessels were thrombosed and showed beginning canalization. Some of the ring hemorrhages contained polymorphonuclear leukocytes, which had a tendency to arrange themselves either at the periphery or at the center. The areas surrounding the ring hemorrhages were pale and edematous. In places some of the distended veins were completely surrounded by polymorphonuclear leukocytes and endothelial and plasma cells. Occasional compound granular corpuscles were also seen. Some of the cortical vessels showed slight proliferation and swelling

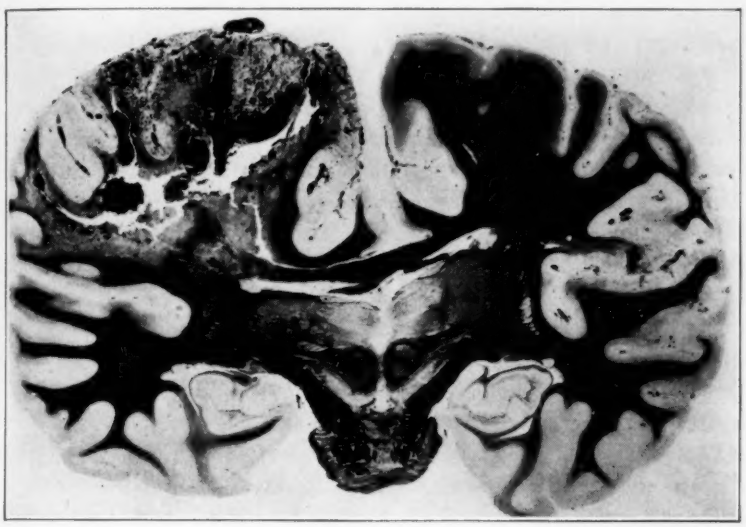

Fig. 4.—Hemorrhages and thromboses of branches of the left middle cerebral vein, with destruction of the left parietal convolutions. Small hemorrhages occur in the right parietal and temporal convolutions. Note the extensive demyelination of the white matter of the left cerebral hemisphere, the ischemia of the right parietal convolutions and the subarachnoid hemorrhages. Myelin sheath stain.

of the endothelial cells. The nerve cells presented loss of Nissl substance and were very pale, while the nucleus and nucleolus stained deeply (ischemia). Some of the nerve cells appeared as shadow cells. Complete destruction of ganglion cells was also noted. In the leg and bladder areas of the right motor region, in addition to the aforementioned changes there was a large collection of compound granular corpuscles. At the periphery of the area of softening, proliferating astrocytes and gemästete cells were observed. Some of the blood vessels in this region showed moderate atherosclerotic changes.

A section through the right gyrus cinguli disclosed a process similar to that in the right motor region.

In a section through the red nucleus (fig. 4), the extensive large and small hemorrhages in the left parietal region and the less extensive process in the right

parietal and temporal convolutions (fig. 4) disclosed histopathologic changes similar to those seen in the sections of the motor region, except that the process and the demyelination were more marked (fig. 4).

In the left occipital convolution the pathologic changes resembled those already described.

Spinal Cord: No abnormalities were noted in the sections stained for myelin sheaths or with cresyl violet.

COMMENT

The essential pathologic changes were thromboses and hemorrhages in the brain in the regions drained by the right and the left middle and posterior cerebral veins. The hemorrhages were recent, being at most about seven days old, as seen by the absence of hemosiderin, which usually appears from about six to ten days after hemorrhage. The histologic examination also indicated that the venous thrombi and hemorrhages were secondary to an infectious and thrombotic process in the dural sinuses, especially in the right lateral and the superior longitudinal sinus. The sequence of events in the pathologic process was most likely as follows: chronic otitis media on the right side, with osteomyelitis of the petrous portion of the temporal bone; thrombosis of the right lateral sinus; retrograde extension of the thrombus into the superior longitudinal sinus, with obstruction of the tributary cerebral veins interfering with the venous, and ultimately with the arterial, circulation of the brain, leading to hemorrhages and softenings. The terminal meningeal reaction and subarachnoid hemorrhages were secondary to thrombosis and rupture of the cerebral blood vessels.

It is generally recognized that damage to the brain produced by obstruction of veins is more diffuse and less intense than that due to arterial occlusion. Putnam and Alexander,[1] Putnam,[2] Bailey and Hass[3] and others have recently studied the pathologic changes in the central nervous system following venous thrombosis. Putnam and Alexander[1] and Putnam[2] also were able to reproduce such changes experimentally. They found that extreme widespread venous obstruction leads to necrosis, chiefly of the gray matter. More limited or gradual occlusion produces extreme stasis and often diapedesis of red and white cells. The affected areas show perivascular zones of demyelination, which may coalesce as damaged myelin is absorbed. In late stages the relative intactness

1. Putnam, T. J., and Alexander, L.: Disseminated Encephalomyelitis: A Histologic Syndrome Associated with Thrombosis of Small Cerebral Vessels, Arch. Neurol. & Psychiat. **41**:1087 (June) 1939.

2. Putnam, T. J.: Evidences of Vascular Occlusion in Multiple Sclerosis and "Encephalomyelitis," Arch. Neurol. & Psychiat. **37**:1298 (June) 1937; Lesions of "Encephalomyelitis" and Multiple Sclerosis: Venous Thrombosis as the Primary Alteration, J. A. M. A. **108**:1477 (May 1) 1937.

3. Bailey, O. T., and Hass, G. M.: Dural Sinus Thrombosis in Early Life, Brain **60**:293 (Sept.) 1937.

of axis-cylinders may be striking. Proliferation of macroglia and oligodendroglia far beyond the area of myelin destruction is more characteristic of venous than of arterial occlusion. Diffuse destruction of cortical tissue is somewhat less common in venous obstruction. Even when the site of obstruction is the pia, the lesions may be more manifest in the white matter than in the cortex. "Maplike" areas of demyelination alternating with relatively normal tissue occur, as in the milder arterial occlusions. On the whole, the type of damage to the nerve tissue appears to be similar to that resulting from the closure of small arteries or capillaries, differing only in extent and distribution. An "inflammatory reaction," consisting chiefly of proliferation of glia cells in the white matter and of hematogenous cells in the gray matter, occurs more often after venous than after arterial occlusion. Essentially the histopathologic changes in our case correspond to those described by Putnam and Alexander.[1]

The clinical diagnosis of otogenous phlebitis is relatively easy when only the lateral sinus is affected and there is evidence of ear disease. The diagnosis is more difficult when the sinus is only partially occluded; in such cases headache and slight fever may be the only symptoms, and even these may be absent. In most cases of otogenous thrombosis of the lateral sinus, however, symptoms and signs of meningitis, brain abscess or extradural abscess may be present. As a matter of fact, perisinus abscess is not infrequently the forerunner of thrombosis. In cases of complete occlusion of the lateral sinus there are usually edema of the tissues and distention of the cutaneous veins in the mastoid region and evidence of extension of the obstruction into the first part of the jugular vein. In these cases compression of the jugular veins during lumbar puncture usually discloses a lower rise of the fluid in the manometer on the side of the obstruction. In some cases of thrombosis of the lateral sinus the lateral movements of the head may be restricted, and at times there may be symptoms referable to the ninth, tenth, eleventh and twelfth cranial nerves on the affected side.

The changes in the cerebrospinal fluid in cases of thrombosis of the lateral sinus vary with the degree of intracranial involvement. In the absence of meningeal involvement the fluid is, as a rule, normal. When the thrombosis is associated with meningitis the changes in the cerebrospinal fluid are those of meningitis, although in some cases, even in the absence of meningeal signs, the fluid may show pleocytosis and a slight increase in protein. Even in so-called otitic hydrocephalus, unless it is accompanied by meningitis or a meningeal reaction, the fluid in most cases is normal, except that it is usually under increased pressure.

The clinical picture of occlusion of the superior longitudinal sinus is indefinite and inconstant. If the occlusion is partial and comes on slowly and gradually, there may be no symptoms indicative of the

disturbance. Generally speaking, the symptoms depend to a great extent on the interference with the circulation in the superior cerebral veins, especially those draining the precentral and postcentral gyri. In cases of more rapid occlusion the usual clinical picture is that of a sudden onset of jacksonian seizures progressing from one foot to the other, or beginning in the foot and gradually involving the homolateral upper limb, usualy sparing the face. In the absence of evidences of meningitis such a symptom complex coming on acutely in a patient with evidences of thrombosis of the lateral sinus secondary to suppurative otitis is generally indicative of retrograde extension of the thrombosis into the superior longitudinal sinus. The association of these symptoms and signs with hydrocephalus and papilledema in the absence of progression or with actual regression of symptoms is strongly suggestive of secondary thrombosis of the longitudinal sinus. The presence of red blood cells in the spinal fluid or the coexistence of a subarachnoid hemorrhage is confirmatory evidence of complete occlusion of the longitudinal sinus. In cases of mural thrombosis without complete occlusion the cerebrospinal fluid is usually normal.

Our patient gave a history of intermittent purulent discharge from the right ear for three years before he came under observation. During this entire period there were neither subjective nor objective evidence of an intracranial complication of chronic ear disease. When he came under our observation he gave a history of sudden onset of a jacksonian seizure of the right leg and weakness of the left arm. The objective neural signs were those of a lesion in each cerebral hemisphere, and, although there were no evidences of meningitis or of intracranial hypertension, the history of tuberculosis suggested the possibility of multiple tuberculoma of the brain. Intracranial injection of air disclosed moderate internal hydrocephalus with no displacement of the ventricular system and more or less symmetric bilateral cortical atrophy. Neither the encephalogram nor the results of examination of the spinal fluid (on alternate jugular compression during lumbar puncture, the rise in the manometer was equal on the two sides) shed further light on the diagnosis. The red blood cells in the first specimen of spinal fluid were attributed to a "traumatic tap." We did not think of primary thrombosis of the longitudinal sinus, i. e., of a marantic thrombus due to the presence of tuberculosis, because the latter was not active and the patient's general condition was excellent. He certainly presented no manifestations of a chronic cachectic state, which is usually regarded as the cause of primary, or marantic, thrombosis. The possibility of secondary thrombosis of the longitudinal sinus was not thought of because of the absence of a general or local process that could be regarded as a cause of secondary thrombosis. The painless chronic discharge from the ear, with a normal mastoid, as demonstrated roentgenographically,

in the presence of evidences of involvement of both motor areas in the brain, was not regarded as a pathogenetic factor in the production of his intracranial symptoms.

Three days before death the patient began to have signs and symptoms of meningeal involvement. It was then thought that, after all, the case might be one of tuberculous meningitis. Although the spinal fluid was under enormous pressure (450 mm. of water) was hazy and had a definite pellicle formation and gave a positive tryptophan reaction, the presence of only 29 lymphocytes per cubic millimeter, the relatively normal sugar content and the absence of organisms in the fluid, as proved on culture and smear, were all against the diagnosis of tuberculous meningitis. The meningeal complication made the diagnosis still more obscure.

A definite diagnosis could not be established until necropsy and the histologic examination of the brain revealed the true nature of the process.

In view of the pathologic findings we gave as our opinion that the patient's intracranial condition and his death therefrom bore no causal relation to the injury which he had sustained on April 23, 1937.

THE GRAPHIC RORSCHACH TEST I

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With the orthodox Rorschach test as a point of departure, the following technic and procedure is suggested as a supplement making scoring as well as interpretation more conclusive. Without suggesting or forcing the limits, it rather allows free efferent response to a specific afferent stimulus.

In cases of mental illness individual responses are difficult to comprehend through the patient's eyes. The graphic Rorschach test allows a controlled stimulus to demonstrate graphically the patient's own perceptions and his responses and how they may deviate from the usual. The more bizarre the response, the more clearly is it demonstrated, the test having application to all types of patients, whether normal or with an organic or functional disorder. Further, the only requirement is a cooperative patient. No technical skill is required. Even patients with verbal facility clarify and add; those without verbal facility make themselves much more understandable.

TECHNIC AND PROCEDURE

The Rorschach record and inquiry are obtained in the usual manner. At a later sitting, each Rorschach card, together with white drawing paper and colored pencils, red, green, yellow, blue, orange and black, is placed before the patient. Stress is laid on this procedure as an attempt to clarify the patient's responses, and not as a measure of his artistic ability.

The object of the procedure is then indicated to the patient by requesting him to draw on paper, with the use of pencils, what he saw on the card. He is asked: (*a*) specifically to point out parts and/or characteristics giving that impression; (*b*) to add what is necessary, if anything, to complete the impression; (*c*) to describe, with a running commentary, what he is drawing, and (*d*) when the present response differs from the previous one, to elaborate the earlier one also, after being reminded of the difference. Spontaneous additions are accepted without comment.

This procedure is carried on uniformly for all ten cards in the presence of the original examiner and the psychiatrist, for the following reasons:

(*a*) The patient is thus given the impression that his ideas are important enough to warrant clarification and that this might perhaps best be indicated by his *drawing* his responses, in addition merely to verbalizing them.

(*b*) This procedure removes from the patient the onus of a test situation associated with the psychologist, who has previously examined him.

(*c*) The technic offers the psychiatrist another avenue by which to establish a means of approaching the patient's guarded preoccupations.

In the cases on which this study is based, the graphic Rorschach test has suggested positive information in ways which may now be discussed under the following heads.

Fig. 1.—Mu.'s graphic Rorschach responses.

I. MANNER OF APPROACH TO THE DRAWING SITUATION

The character of the actual drawing is illustrated by the following examples.

1. Patient Mu.'s drawings consisted of bold and careless lines, were loose and exhibited marked left asymmetry (fig. 1). No attempt at accurate definition of the impression could be noted, and there was conspicuous lack of concern with detail. Descriptively, the patient is aggressive, domineering, positive, dogmatic and impulsive.

2. Patient C.'s drawings had vague, light lines and nebulous qualities, were sketchy and unconnected, but outlined a definite idea (fig. 2*A*).

The drawings were unfinished. Descriptively, the patient is ineffectual, passive and schizophrenic, his illness being in a period of remission.

3. Patient R. showed a timid approach, delicate and replete with concern for detail. The drawings are completed projects leaving little to the imagination (fig. 2 *B*). Descriptively, the patient, who has a manic-depressive psychosis and is recovering from a depression, is timid, with many attempts at compensations, very precise, meticulous, compulsive and highly intelligent.

II. STABILITY OF PERCEPTIONS

How clear are the perceptions, and are they the same after an interval? In 1 case drawings were made on the same day. In another there was a one month interval. The average interval was three to seven

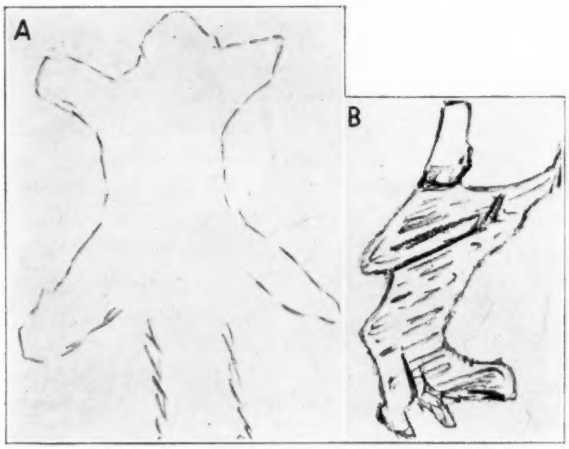

Fig. 2.—(*A*) C.'s and (*B*) R.'s graphic responses.

days. If perceptions are fleeting, this is demonstrated in the drawings. If they are fixed and clear, this is also revealed.

III. ACCURATE QUANTITATIVE SCORING AND TABULATION

Where scoring was done on the original record without drawings, there were some misconceptions as to the exact use which the patients made of the stimulus cards. Other scorings were strongly confirmed.

A. Location of Responses.—1. Gross Location: Is it a "whole," a "cut-off whole," a "primary detail," a "secondary detail," a "rare detail" or a "space" response?

2. Amount of Concern with Detail in Elaborating the Responses: For example, in a "whole" response does the patient include details representing definite parts, or does he give only the general outline? Two patients gave "butterfly" responses to card I, scoring W, FM,

A and P. One drew a center line for the body and two squared projections for the wings (fig. 3 *A*). The second patient indicated details of the shaping of the wings, the place where the antennae would be, the place where markings would be, etc. (fig. 3 *B*). Here one gets an indication of the richness of the percept.

3. Spontaneous Additions to Complete the Picture: This is the same general principle as that indicated in the preceding section. What does the patient add to the card to complete the percept, and how concerned is he with its completion? For example, in the response to card I, which he described as "a dancer spinning with veils," patient M. added a head to the dancer and elongated the proportion of the central body figure to make it more attractive (fig. 4 *A*). Another patient, Mn., used the outlines of card III for the "head of a gorilla" and did not indicate the limit of the top of the head, there being no line at that point on the card (fig. 4 *B*).

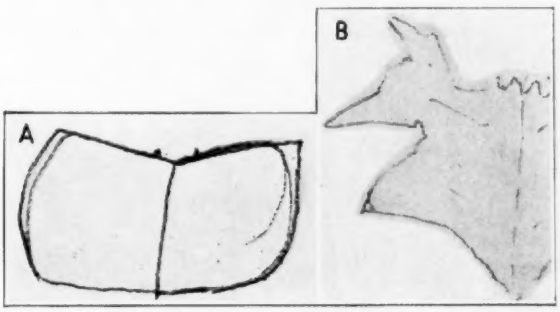

Fig. 3.—Graphic modifications of two patients of the "butterfly" response to card I.

4. Degree to Which Impressions Are Related to the Stimulus Cards: This is another aspect of the point discussed in paragraph 3. In some cases the card or its parts are used for a portion of a response, a large part of which is supplied imaginatively. For example, patient C. pointed to portions of the head and trunk of the usual "men" in card III and said, "heads of two bears." The drawing reveals that these sections were used as portions of the snout and ears and that the rest of the head contour was supplied by imagination in the white space (fig. 5 A).

B. Determinants Used.—In those cases in which several determinants play a part, scoring is considerably easier if one knows the relative importance to be ascribed to each.

1. Movement: Movement, human and animal, is obviously much clarified by the graphic method, with its commentary.

2. Form: The distinction between good and poor form level (F plus and F minus) is a great deal easier. Many patients respond to

card VI with "birds" or some other winged creature; without drawings, however, it is difficult to know whether this is one of the more usual forms of response or a novel use of the card properties.

3. Color: Determination of the importance of form in combination with color is one of the greatest difficulties of scoring with only a verbal report from the patient. In other words, is a response to be scored FC, CF or C? A large proportion of the discrepancies between scoring assigned on the basis of verbal report alone and that on the basis of additional graphic representation were in the sphere of color answers. For example, patient M. responded to card VIII with "cross section of some flower, a rose bud," adding in the inquiry, "The color should be reversed

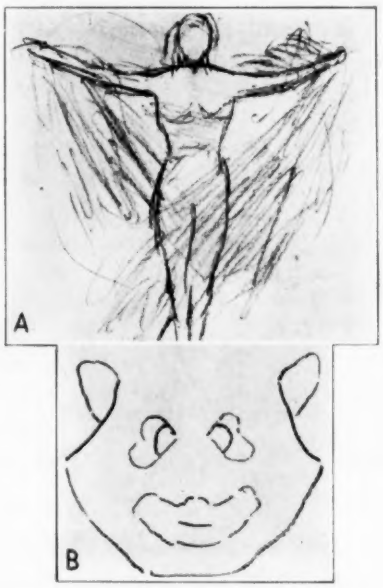

Fig. 4.—*A*, L.'s graphic response to card I; *B*, Mn.'s graphic response to card III.

here." This seemed to indicate that recognition of color had played a part, although secondary to form, and the response should be scored FC. In drawing, he refused to use the colored pencils (although he used them freely in other drawings) and portrayed the concept in terms of form alone (fig. 5 *B*). Another patient, who in all other cards had followed the form outline of the blots closely in his drawings, responded to card IX with "some kinds of shoots or flowers." In this one drawing he completely departed from the form given in the blot and sketched a schematic design with the three colors in the positions they occupy on the card (fig. 6 *A*); this demonstration of the weakness of the form perception in combination with color would have been difficult to grasp

by any other method than the graphic, particularly since it was in sharp contrast to his performance on all other cards.

4. Shading: The same problems of scoring discussed with reference to color enter into the scoring of the shading responses. That is, to what extent is shading important in combination with form? The drawing leaves no doubt in the matter. Patient R. described card II as "Cossacks prancing, Cossacks because they have red hats," and *only* in the drawing did his response of "their shaggy bearskin coats" illustrate his inclusion of shading (fig. 2*B*). Another patient, giving a common animal response to card IV (usually including texture), denied all use of texture in his drawing and based his illustration entirely on form.

C. Popular Level and Original Responses.—Original additions or elaborations to popular responses are not always easily determined from verbal description alone, although the factor of popularity itself is rela-

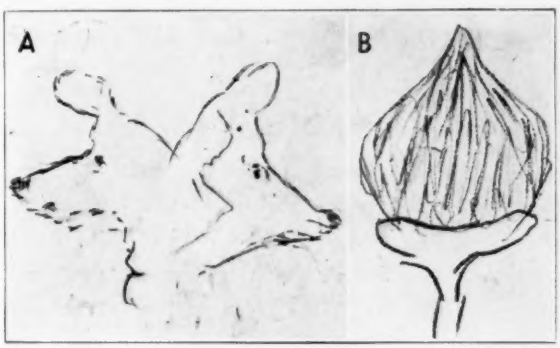

Fig. 5.—*A*, C.'s response to card III; *B*, M.'s response to card VIII in terms of form alone.

tively easy to discern. The following classes of responses must necessarily be evaluated: (1) The simple popular response; (2) the popular response with original additions; (3) the original and well elaborated response, and (4) the original response of poor quality, which is of diagnostic significance in pathologic conditions.

IV. ACCURATE QUALITATIVE EVALUATION OF THE RECORD

A. Demonstration of the Pathologic Qualities of the Record—1. "Contaminatory," "Fabulatory" and "Confabulatory" Responses: These types of responses, by virtue of their bizarre quality, lend themselves to nebulous description on the part of the patient and to incomplete comprehension on the part of the examiner. The technic presented here offers the first opportunity to examine these responses carefully in a graphic form which lends itself to analysis and scoring and thus defines the nebulous quality and uncertainty of the patient's idea. For example,

patient K. responded to card VII: "That's either a man or woman in different positions, more like a woman," adding in the inquiry, "This is what makes me believe it's a woman (pointing to the center dark detail). She's laying down; her legs going up like this." Drawing revealed that the detail indicated had been interpreted as the vaginal entrance and that the remainder of his sketch depicted a woman with legs in extreme flexion, the contours bearing no relation to the shape of the blot beyond their general placement on the card.

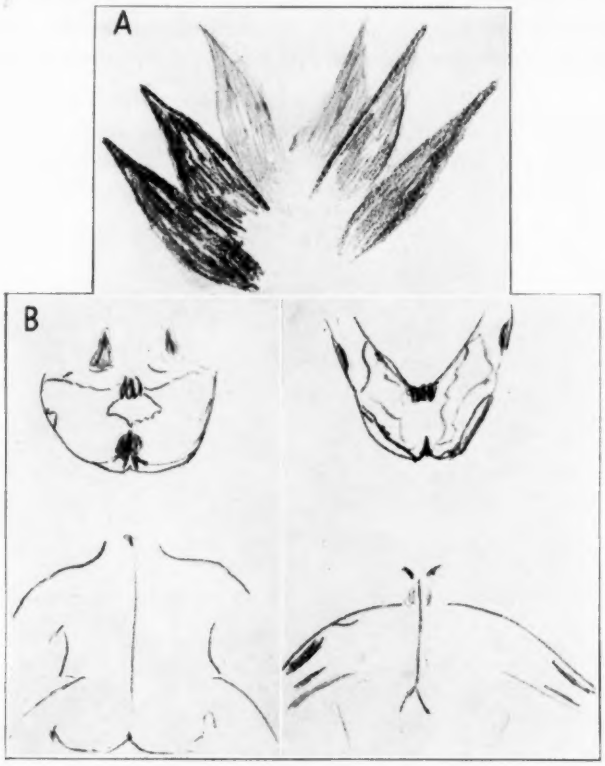

Fig. 6.—*A*, schematic design of the three colors in card IX; *B*, K.'s Rorschach responses.

2. Weak Use of Color (superficial or "empty" emotionality): As described in the foregoing discussion of color responses, the exact quality of the use of color is readily demonstrable. In the case of patient M., whose response to card VIII has already been described, the Rorschach interpretation of a forced superficial emotional adjustment to the social world supported strongly the clinical picture of "emptiness."

3. Perseveration and Stereotypy: Verbal responses frequently mask the extent and, again, the specificity of such phenomena as perseveration

or stereotypy. Patient K. (see appended case study) revealed a monotopical concern with "human X-ray" in his responses to all ten cards, stating this preoccupation quite differently in each. In the graphic Rorschach test, however, these superficially related productions became conspicuously stereotyped, perseverative and repetitive, to the extent that the drawings were almost identical in all details.

4. Autistic Thinking: This was particularly clearly defined in the case of patient K., described in section 3. The identity of the ten drawings was so great that the presence of a fixed idea related to his sexual preoccupation was established beyond a doubt, and would not have been otherwise apparent. His responses were thereby shown to be even less well related to the individual cards than they had seemed to be in his original verbal statement.

We have thus probably recorded the schizophrenic mechanism of being able to take a real stimulus and fantasy beyond it. The drawings tend to form an index of the patient's ability to use fantasy, or what we have chosen to designate as an "autistic index."

V. RELATION BETWEEN "ORTHODOX" VERBAL RECORD AND GRAPHIC RORSCHACH RESPONSE

In almost every case more responses were given at the time of the graphic Rorschach test than in the original record, and in certain cases responses given originally were denied at the time of drawing. The spontaneous additions seemed to represent a more free and less inhibited performance than was obtained with purely verbal responses. Patient M., a patient of very superior intelligence in an early stage of schizophrenia, had given a record of ten responses, with only one scored M and one scored FM. At the time of drawing, he produced twenty-four additional responses, of which seven were scored M and four FM. In this case, it seems that the drawing actively released an efficient mental productivity commensurate with his intelligence which had not appeared in his earlier responses.

VI. ILLUSTRATIVE CASE RECORD

Patient K., a native American aged 26, gave no positive evidence of the presence of chronic contagious disease or nervous or mental illness in the family other than that the father is the dominant member of the family, all of whom have mercurial temperaments. One sibling, who had a disturbance of the thyroid, also had a period of illness somewhat like the patient's. There has been no outstanding intrafamilial difficulty.

The birth and early development of the patient are reported to have been normal. He had the usual illnesses of childhood, without complications. He graduated from high school with honors at the age of 17.

He has long been recognized as an unusual member of the family, having specific personality defects which had manifested themselves since an early age, chiefly marked sensitivity and feelings of inferiority and inadequacy, which he

attempted to overcome by aggressive, rigid, domineering behavior patterns. With time these modes of behavior gave rise frequently to argumentativeness, which often interfered with the quality of his work.

The patient was married six months prior to admission to a girl he had known for some years. Their marital life, thus far, continued without serious manifested difficulty, though the wife had noted early that the patient characteristically "kept things from her" (a typical behavior expression the family had long recognized).

The present illness had its frank onset ten days prior to admission. At work he had given evidence of suspiciousness and came home expressing ideas of reference, which gradually grew to include the family. At the same time fragmented sleep and some loss of weight were noted. However, physical examination revealed nothing abnormal. Laboratory data were also well within normal limits. On psychometric examinations he obtained a mental age rating of 14-4 and an intelligence quotient of 90, which, in view of the school achievement, were not considered representative.

During hospitalization, he adjusted poorly to the hospital routine, at times becoming impulsive and assaultive and expressing ideas of reference toward other patients and distrust toward members of the staff other than the examiner. Within a short time the latter, too, had become included in his delusional system.

Until the graphic Rorschach test had been carried out it was impossible to obtain an inkling of his fundamental preoccupations. Repeated psychiatric examinations in the usual manner were fruitless. Evasiveness and suspiciousness were evident, but no significant content was elicited.

A Rorschach record was obtained two weeks after admission. A representative portion of his Rorschach protocol is submitted along with his corresponding graphic Rorschach record, which was obtained four days later.

Card	Time, Min.	Original Response	Inquiry	Comments Made During the Graphic Rorschach Test
II.	49″ 1.	I know but I'd rather not say (reassured by E). Looks like the woman's bottom.	This would be the entrance and this the cavity. X-ray. She's in her period.	This is only a space left by the X-ray. These are blood spots inside.
III.	5″ 1.	Practically the same as the other.	This (center D at bottom) and these two red spots, they're an X-ray of blood.	These are blood spots and the leg is up. These are bones in the body.
IV.	12″ 1.	Could be an X-ray of somebody sitting down.	Legs outstretched. These seem to be shoulder muscles. Parts of his feet. Here's a closing up in his throat. X-ray of a woman's hips. Sort of wide here	Shoulders here—legs outstretched. This is the spinal column. This is the throat. These are X-rays of the bones in the body.
V.	3″ 1.	X-ray of man or woman with arms out like this.	These are bones in the wrist. Shoulders here. These are two bumps on shoulders. These are jawbones.	Jawbones. These are shoulder bones. Here is the spinal column. These are two little bones in back. These spaces are the marrow inside.

During the graphic procedure, the patient gave a running commentary as he drew his impressions of the cards. Specimen drawings are presented (fig. 6*B*).

The day following completion of the graphic Rorschach test the patient was interviewed by the psychiatrist; the drawings were laid out before him. The examiner commented that they revealed a concern with matters which he had not, as yet, communicated. It was further mentioned that these drawings showed a trend toward uniformity which was enhanced when some of them were turned upside down. He then, spontaneously, began to reveal, somewhat evasively, that he was concerned with his sexual activities in relation to his wife. This discussion formed the first basis for such intimate comment, beyond the superficial ones of previous interviews. This session with the patient thus provided a beginning for a subsequent series of more satisfactory and significantly productive ones.

COMMENT

The aforedescribed method gives evidence of both positive and negative significance. In those records in which the series of drawings exactly parallels the verbal response, the original scoring is confirmed and verified, thus providing a simple and conclusive check. In those records in which the graphic results not only parallel the verbal response but give evidence of additional material, it is possible to arrive at a more accurate scoring and interpretation, having both qualitative and quantitative value.

In the usual Rorschach procedure, the verbal response to the visual stimulus perforce places the former in a different sense modality. The graphic Rorschach test makes it possible for the response to be expressed in the same sense modality as the stimulus; this method provides the Rorschach test as a more completely projective technic.

There are several possible applications of the method to fields not yet thoroughly investigated. The realm of organic disorders offers almost unlimited possibilities. Several important characteristics of the patient with organic disease, particularly his typical difficulty in locating his perceptions with reference to the blots, is especially easily demonstrated by this means. In cases of a speech defect (for example, the aphasias) the graphic method helps the patient bridge the language gap and gives a more accurate Rorschach record because it eliminates partially the dependence on words.

Children's drawings have long been recognized as having an expressive function and assume now a new significance, since the verbal Rorschach response of children is notoriously less well elaborated than is that of adults. A method which obviates total dependence on verbal response and which includes an expressive medium used particularly freely by children makes more accurate work in this field possible.

In the drawings of this group there was a suggestion that in some cases the representations had a significant symbolic value over and above

the other characteristics. The possibilities of this sphere of investigation warrant pursuit in a study devoted to such productions.

CONCLUSIONS

1. An original graphic technic and procedure is described which is designed to act as a confirmation, supplement and extension of the Rorschach method.

2. Case material is cited to show certain advantages of the graphic Rorschach test.

(*a*) The method allows the patient's Rorschach responses graphic representation without the necessity of technical skill.

(*b*) More accurate quantitative and qualitative evaluation of response records is exhibited.

(*c*) Graphic demonstration of the pathologic qualities of records where they exist is facilitated.

(*d*) The record including the graphic response tends to be fuller and less inhibited and therefore to elicit trends not as clearly expressed by the orthodox procedure.

(*e*) Simultaneous examination of concepts as distinct from individual precepts is demonstrated.

3. Implications for further work in related fields are indicated.

The staff of the Fairfield State Hospital cooperated in this study.

ELECTROENCEPHALOGRAPHIC EFFECTS OF ACUTE INCREASES OF INTRACRANIAL PRESSURE

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AND

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During the past decade the examination of the electrical activity of the cerebral cortex has become of value in clinical neurology. Various studies have shown that a pathologic condition is usually indicated by the presence of slow waves of increased amplitude in the electroencephalogram. Berger [1] stated that these slow waves were entirely due to increased intracranial pressure. Walter [2] observed that there was no correlation between the intracranial pressure and the character of the electroencephalogram. Williams [3] made a further analysis of the problem and concluded that changes in the electrical activity of patients with increased intracranial pressure were due primarily to intracellular hydration of the white matter and not to the raised pressure per se. Hoagland and his collaborators,[4] studying the problem in dogs, found no change in the electrical activity when the intracranial pressure was increased to approximately 25 mm. of mercury.

The present experiments were performed to determine the effects on the electroencephalogram of rapid increases of intracranial pressure to heights above that usually encountered in clinical practice.

METHOD

In these experiments 4 cats, 4 dogs and 2 monkeys (Macaca mulatta) were studied. Surgical anesthesia was induced by intraperitoneal injections of pento-

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From the Laboratory of Physiology, Yale University School of Medicine.

Read at the meeting of the American Physiological Society in Chicago, April 19, 1941.

1. Berger, H.: Ueber das Elektrenkephalogramm des Menschen: Dritte Mitteilung. Arch. f. Psychiat. **94**:16-60, 1931.

2. Walter, W. G.: Critical Review: The Technique and Applications of Electroencephalography, J. Neurol. & Psychopath. **1**:359-385, 1938.

3. Williams, D.: The Abnormal Cortical Potentials Associated with High Intracranial Pressure, Brain **62**:321-334, 1939.

4. Hoagland, H.; Himwich, H.; Campbell, E.; Fazekas, J., and Hadidian, Z.: Effects of Hypoglycemia and Pentobarbital Sodium on Electrical Activity of Cerebral Cortex and Hypothalamus (Dogs), J. Neurophysiol. **2**:276-288, 1939.

barbital sodium or sodium amytal. Deep barbiturate anesthesia diminished the rise in blood pressure associated with increased intracranial pressure, thus rendering accurate the correlations between pressures and brain waves. A tracheal cannula was inserted, and whenever respiratory failure appeared imminent artificial respiration was employed to prevent lowering the oxygen tension of the blood. Midline scalp incisions were made; the skin, galea and temporal muscles were reflected bilaterally, and a 1 cm. trephine opening was made over the left frontoparietal region. The dura was incised radially, and a fitted cannula was tightly screwed into the trephine opening. This cannula was attached to a pressure bottle containing physiologic solution of sodium chloride and to a mercury manometer. Blood pressures were recorded from the right femoral artery by means of a mercury manometer. The anticoagulant agent used was sodium citrate or chlorazol fast pink.

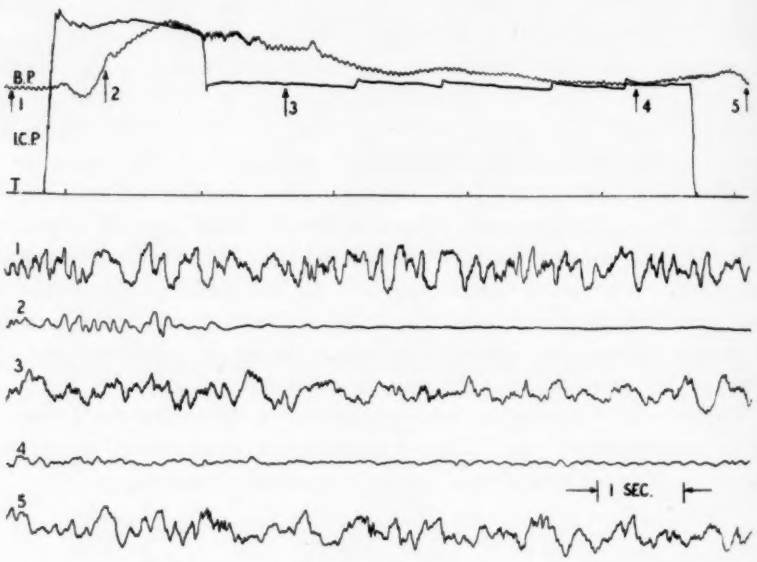

Fig. 1.—This chart demonstrates that the cortex becomes electrically silent when the intracranial pressure exceeds the blood pressure and that the activity reappears when the intracranial pressure level is subsequently lowered below the blood pressure level.

The monkey was under light amytal anesthesia. *B.P.* indicates blood pressure, and *I.C.P.* intracranial pressure; *T* records time in minutes and is also the base line for both pressures. Arrows and numbers *1-5* on the kymograph record indicate points of sampling for the corresponding electroencephalographic tracing.

The electroencephalograms are bipolar, push-pull records from the left cortex, taken with constant gain and filters. *1* is a record taken before intracranial pressure was increased; *2* was taken thirty seconds after pressure was increased; *3*, forty seconds after reduction of the pressure; *4*, thirty seconds before reduction of the intracranial pressure to zero, and at the time when the level of the blood pressure was approximating that of the intracranial pressure, and *5*, thirty seconds after the intracranial pressure was reduced to zero.

Leads were attached to electrodes placed directly on the cleaned bone or to screws driven into the skull over the frontal and parieto-occipital regions bilaterally. Push-pull records were taken from each hemisphere by two channels of a three lead, ink-writing oscillograph. Heart records were continuously recorded by the third lead. Changes in the heart record gave evidence as to advisability of maintaining the pressures.

RESULTS

The results of these experiments are graphically portrayed in the accompanying three figures. Figure 1 depicts the changes produced in the electroencephalogram by increasing the intracranial pressure to a height above the blood pressure level. The cortex becomes electrically silent within ten to forty seconds after this occurs. The reversibility of this effect is evidenced by the return of electrical activity when the intracranial pressure is reduced.

Figure 2 demonstrates the effects of successive increases of intracranial pressure to heights above the prevailing blood pressure. The

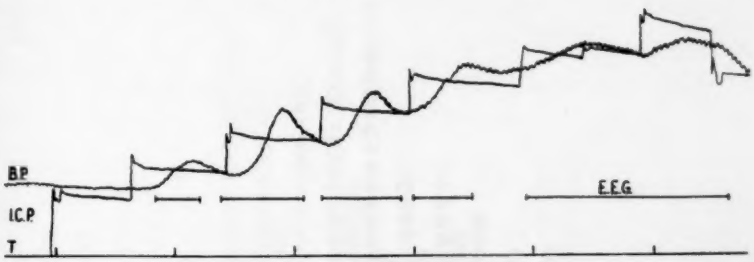

Fig. 2.—This demonstrates the effects of successive increases of intracranial pressure to above the blood pressure level and of the concomitant rises of blood pressure. The cortex becomes electrically silent when the intracranial pressure is higher than the blood pressure, and the electrical activity reappears when the intracranial pressure is lower than the blood pressure. The absolute level of the intracranial pressure is not correlated with the presence or absence of electrical activity.

The monkey was under light amytal anesthesia. *B.P.* indicates blood pressure, and *I.C.P.*, intracranial pressure; open spaces in the line *E.E.G.* indicate presence of cortical, electrical activity; *T* records time in minutes and is also the base line for both pressures.

brain waves disappear when the intracranial pressure exceeds the blood pressure, and this is indicated by the presence in the figure of the solid line. The cortex again becomes electrically active if Cushing's phenomenon [5]—rise in blood pressure in response to increased intra-

5. Cushing, H.: Physiologische und anatomische Beobachtungen über den Einfluss von Hirnkompression auf den intracraniellen Kreislauf und über einige hiermit verwandt Erscheinungen, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **9**:773-808, 1902.

cranial pressure—is sufficiently prolonged. This phenomenon occurs when the cortex is electrically silent. There is no correlation between the absolute level of the intracranial pressure and the electroencephalographic changes.

Figure 3 presents the correlation for all experiments of the difference between the intracranial and the blood pressures, on one hand, and the electroencephalographic changes, on the other. When the intracranial pressure is less than the blood pressure by 40 or more mm. of mercury no change in the electrical activity occurs. When the intracranial pressure equals or exceeds the blood pressure the cortex becomes electrically silent. In the intermediate range a decrease in amplitude and a loss of higher frequencies in the electroencephalogram are seen. This decrease in both frequency and amplitude is noteworthy, as in the presence of a pathologic condition a decrease of frequency is usually associated with an increase of amplitude (Gibbs and Gibbs [6]).

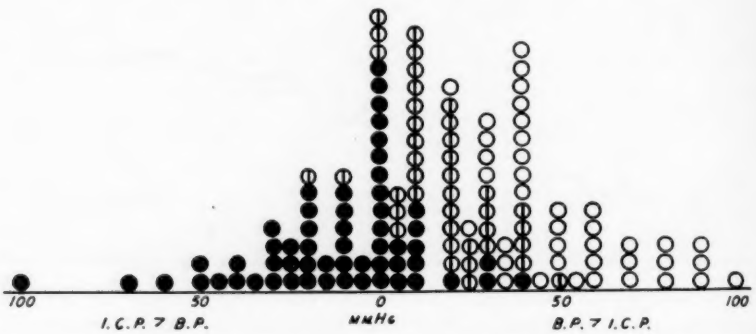

Fig. 3.—This summarizes all observations on the differences between the intracranial and the blood pressures and the electroencephalographic changes. On the right side of the diagram the blood pressure is greater; on the left the intracranial pressure is greater. The hollow circles represent an unchanged electroencephalogram; the circles with line, a decrease in amplitude and frequency in the electroencephalogram, and the solid circles, absence of electrical activity of the cortex.

CONCLUSIONS

Since the electroencephalographic changes which have been described here are dependent on the relationship between the intracranial and the blood pressures, it is evident that these effects of acute intracranial hypertension are the result of impairment of blood flow. That the pressures used in these experiments which produced an effect on the cortical electrical activity lie for the most part beyond the realm of those

6. Gibbs, F. A., and Gibbs, E.: Atlas of Electroencephalography, Cambridge, Mass., Lew A. Cummings, 1941.

pressures recorded clinically is obvious. Merritt and Fremont-Smith [7] in 167 patients with brain tumor found pressures no higher than 700 mm. of water. Williams [8] could induce pressures no higher than 500 mm. of water in his subjects.

Therefore it is unlikely that modification of the electroencephalogram in most patients could be ascribed to the intracranial pressure. Other factors must be responsible for such changes, as was concluded by Walter [2] and Williams.[3]

SUMMARY

1. The electroencephalogram is altered by acute rises of intracranial pressure only when the increases are sufficient to alter cerebral blood flow.

2. The pressures required for these acute effects lie for the most part beyond those of clinical experience.

3. Cushing's phenomenon (rise in blood pressure in response to increased intracranial pressure) occurs in the absence of electrical activity of the cortex.

7. Merritt, H. H., and Fremont-Smith, F.: The Cerebrospinal Fluid, Philadelphia, W. B. Saunders Company, 1937.

TWO MINUTE CLINICAL TEST FOR MEASUREMENT OF INTELLECTUAL IMPAIRMENT IN PSYCHIATRIC DISORDERS

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One of the prime necessities for the clinical psychiatrist in the completion of a mental examination is a quickly applicable and reasonably accurate test for the measurement of intellectual efficiency and the estimation of the degree of mental impairment. Most of the available psychologic tests are time consuming and require special technics, and not infrequently special training, for their application. The serial subtraction of 7 from 100 has been found to fulfil the essential requirements, and the purpose of this paper is to establish the standardization and thus to provide a basis of comparison for the results, which heretofore have been impressionistically interpreted. The successful performance of the test depends on the subject's ability to comprehend and utilize simple mathematical concepts involving symbolism and abstractions. As such, in addition to factors of memory and learning, it requires particularly abstract thinking ability. In a previous paper [1] the evolution and development of the comprehension of mathematical concepts were outlined both phylogenetically and ontogenetically and the position of the serial 7 test in such evolution was pointed out.

BACKGROUND

Since the study by Babcock[2] in 1930 a variety of tests have been developed for the measurement of deterioration. Her test, however, consisting of a group of memory, learning and motor ability items, remains the most widely used index of mental efficiency. These functions show the major involvement in any process of deterioration and when compared with vocabulary efficiency, generally agreed to be the best preserved ability, give a relative measure of the subject's intellectual impairment. Although some of the items were concerned with abstract thinking ability, they were not primarily a measure of this function. Specific tests for abstract thinking ability included those of

From the Neuropsychiatric Institute of the Hartford Retreat.

1. Hayman, M.: The Use of Serial Sevens in Psychiatric Examination, Am. J. Orthopsychiat. **11**:341 (April) 1941.

2. Babcock, H.: An Experiment in the Measurement of Mental Deterioration, Arch. Psychol. **18**:68, 1930.

Bolles,[3] Weigl,[4] Cameron,[5] Bolles and Goldstein [6] and Kasanin and Hanfmann.[7] These dealt with the formation of artificial concepts through the arrangement of various types of sorting materials. More recently Shipley [8] has devised a test of the pencil and paper type specifically designed to measure abstract thinking ability. It consists of problems necessitating the induction of a principle and its application. It was found in testing both persons with organic and persons with nonorganic mental disorders that abstract thinking ability as indicated by this test suffered considerably and a fairly sensitive indication of mental deterioration was obtained. While serial subtraction of 7 from 100 does not involve the introduction of new principles, it does measure the subject's ability to handle previously learned abstractions and mathematical concepts, since numbers are symbols used as abstract measures of quantity. Instruction in arithmetical procedures increases facility and directs the choice of method, but the ability to perform simple subtractions will develop when the subject has comprehended the preliminary arithmetical concepts. Most persons with or without educational advantages are constantly exposed to such simple mathematical problems.

METHOD

Administration.—The test is administered orally, the subject being asked to take 7 away from 100, to take 7 away from the answer obtained, and so on. The subjects are placed as much at ease as possible and encouragement is freely given, but no assistance.

Scoring.—Each subtraction is considered as a unit, and calculations are made on the basis of the 14 possible correct subtractions, that is, 93–86–79–72–65–58–51–44–37–30–23–16–9–2. Answers more or less than 14 were proportionally reduced or increased to this figure; for example, 5 correct responses out of 10 would give a raw score of 7 on the basis of 14. Similarly, if 16 subtractions resulted, with 5 incorrect, the raw score would be 4.4. A minimum of 5 responses is considered necessary for the purpose of scoring.

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3. Bolles, M.: The Basis of Pertinence, Arch. Psychol. **30**:51, 1937.

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7. Kasanin, J., and Hanfmann, E.: A Method for the Study of Concept Formation, Am. J. Psychiat. **95**:35 (July) 1938.

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Timing.—It was found in the examination of a group of 333 normal school children that the shortest time taken was thirty seconds and the longest three hundred and fifty seconds, with a mean of one hundred and ten seconds. In the group of psychotic subjects the shortest time required was eleven seconds and the longest four hundred and twelve seconds, with a mean of eighty-four and eight-tenths seconds. Ninety and five-tenths per cent of the patients gave their answers within one hundred and twenty seconds. Calculations are made on the basis of the actual number of subtractions, so that a maximum limit of two minutes can be arbitrarily set. Time determinations might give finer indications of differential abilities, but these were found unnecessary for the purposes of the test.

Patterned Responses.—It was found in the course of the examination of normal school children that 18.2 per cent gave a patterned type of response. These occurred for the most part in the lower age groups and at the lower intelligence levels. The responses followed a number of different patterns, as follows:

A. Repetition of terminal digit.

93-83-73-63-53-43-33-23
7-10-10-10-10-10-10-10

B. Repetition of alternate terminal digit.

93-80-73-60-53-40-33-20
7-13—7-13—7-13—7-13

C. Repetition of terminal digit of three successive responses.

93-86-80-73-66-60-53-46
7—7—6—7—7—6—7—7

D. Miscellaneous responses.

92-96-93-94-92-91-92-90
8-+4—3-+1—2—1-+1—2

or 93-92-91-90-89-88-87-86
7—1—1—1—1—1—1—1

or 93-93-93-92-92-92-91-91
7—0—0—1—0—0—1—0

Group D is a miscellaneous one which includes repetition of the first digit, repetition of both digits and descent by subtraction of 1. These patterns were sometimes complete, appearing throughout the whole range of the test, and sometimes partial, the subject beginning or terminating the test with the repetitive form. Three successive repetitive answers were required for inclusion in the patterned type, since fewer

than this might be purely fortuitous. Table 1 shows the distribution of the patterned responses among the mental age groups, and table 2 indicates the frequency of occurrence and the median error score for each type.

STANDARDIZATION

Mental age norms were established by administering the test to 433 pupils from several different schools. The subjects varied in chrono-

TABLE 1.—*Patterned Responses, Median Error Scores and Equivalent Mental Ages for Responses to Serial 7 Test in a Group of Four Hundred and Thirty-Three School Children*

Mental Age	No. of Children	Median Error	Subjects Unable to Respond	Patterned Responses				Total
				A	B	C	D	
8	51	9.1	10	14	5	3	2	24
9	62	5.4	3	7	4	1	4	16
10	58	4.5	2	5	4	1	2	12
11	70	3.8		3	4	2	4	13
12	68	2.9		2	4	2	....	8
13	45	2.4		1	1	2	....	4
14	45	1.4		....	1	....	....	1
15	26	.7		....	....	1	....	1
16	8	0						
Total	433		15	32	23	12	12	79

TABLE 2.—*Distribution of Patterned Responses and Their Median Error Scores for Normal (433) and for Psychotic (900) Subjects*

Type	Median Error of Normal Subjects	No. of Normal Persons	No. of Psychotic Patients
A	10.4	32	93
B	7.0	23	35
C	4.5	12	11
D	9.5	12	....
Total		79	139

logic age from 8 to 15 years and in mental age from 8 years to 16 years 8 months. Grades 2 to 8 were represented. The intelligence tests used in establishing the mental age equivalents consisted mainly of the revised Stanford-Binet test (form L) and the Otis self-administering test of mental ability (intermediate examination). Median error scores were used in establishing these mental age equivalents. Table 1 shows the error scores and the equivalent mental ages. Figure 1 indicates this in graphic form, and the corresponding mental age with the given error score can be read directly from the graph. It will be noted that above the mental age of 15.9 years no errors were made and that at the lower

portion of the scale the errors showed a marked and disproportionate increase. Within these limits, however, a coherent and integrated picture can be observed.

VALIDATION

Reliability.—Measures of reliability were obtained from two groups. Group 1 consisted of 91 patients with various types of mental disorder who were in a static stage of their illness and whose clinical condition showed little fluctuation. Original testing gave a variation in error scores from 0 to 13, with a mean of 3.2, and retesting showed a range

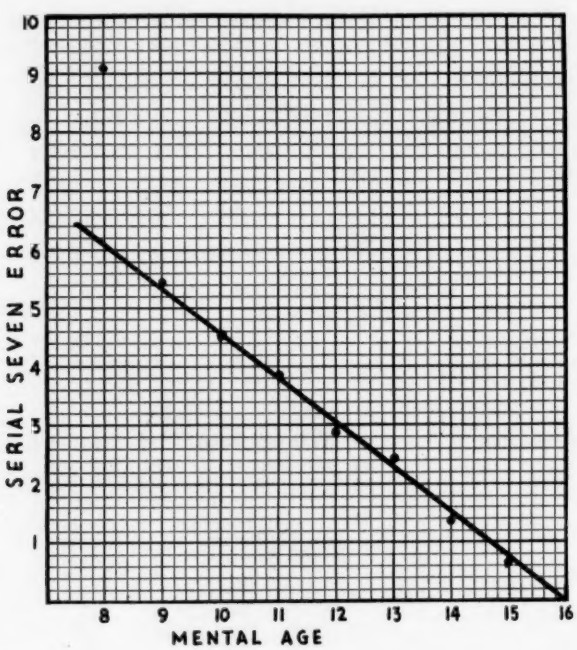

Fig. 1.—Error scores for the serial 7 test and equivalent mental ages.

of error scores from 0 to 12, with a mean error of 2.9. The coefficient of reliability in this series was found to be as follows:

$$r_{xy} = 0.892, \text{ with a probable error of } \pm 0.032$$

Group 2 consisted of 112 normal school children. Original testing in this group showed a range in error score from 0 to 10, with a mean error score of 3.3, and retesting gave a range of 0 to 12, with a mean of 3.1. The coefficient of reliability in this series was as follows:

$$r_{xy} = 0.906, \text{ with a probable error of } \pm 0.029$$

Validity.—No coefficients of validity were obtained, but the evidence from the examination of persons with various types of mental disor-

ders indicates that the test is a useful instrument for the estimation of intellectual efficiency. The error scores of psychotic patients were consistently greater than those of normal subjects, and when the subjects in one diagnostic category were graded according to the clinical severity of their disease, the error scores showed a progressive increase.

Comparison with Other Technics.—In another paper [9] the test was compared with the Shipley-Hartford scale and the Babcock efficiency index and the implications discussed. The coefficients of correlation were:

Shipley-Hartford Scale: 0.797, with a probable error of ± 0.048

Babcock test: 0.702, with a probable error of ± 0.051

These would suggest that the serial 7 test measures factors somewhat more closely allied to the abstract thinking abilities of the Shipley-Hartford scale than the memory, learning and motor ability items of the Babcock test.

INTERPRETATION

Error Score.—The mental age obtained from a given error score indicates that the subject tested is able to do as well as a normal child of that age with respect to the serial 7's. It does not imply that all of the subject's thinking is at that level, nor does it indicate permanency of impairment. It does, however, give one an index of the subject's present facility in handling the abstractions implicit in this problem. If a subject attains an error score of zero (with a mental age of 15.9 years), his performance is normal within the limits of this test. If errors are made, in order to obtain a relative figure to indicate disparity between past and present efficiency, one may utilize the factors in the past history, including school record and grade attained, or the test may be combined with any standard vocabulary test, the latter measuring the function least involved in any process of impairment. This might be expressed, as in the Shipley-Hartford scale,[10] in percentages of normal.

Patterned Responses.—In cases of normal children in which the arithmetical concepts are not clearly defined and the problem is too difficult for the child to solve, there is a tendency to answer by similar sounds, which is continued over subsequent responses by the mechanism of perseveration. Thus there are involved two primitive reactions which are normal in young children: sound associations depending on superficial external similarities, and perseveration. The patterned responses

9. Hayman, M.: A Rapid Test for Deterioration with Comparison of Three Techniques, J. Gen. Psychol., to be published.

10. Shipley-Hartford Scale for Measuring Intellectual Impairment: Manual of Directions, 1940, Neuropsychiatric Institute of the Hartford Retreat, Hartford, Conn.

of persons with mental disorders were identical with those obtained from normal children, which suggests that the failure to comprehend and utilize arithmetical concepts in the child shows a marked similarity to the disorganization in persons with psychoses. Also involved is a confusion between addition and subtraction, with substitution of the former for the latter. The use of addition represents a "regression" to an easier, earlier and more thoroughly learned procedure. In cases of the psychoses the occurrence of patterned responses may be interpreted as the result of suspension or diminution in function of the higher cerebral centers with the reappearance of primitive modes of thought, such suspension or diminution of consciousness decreasing the normal inhibitory effect on stereotypy and perseveration. It will be noted that the completeness of consciousness or awareness appeared to be the determining factor in the frequency of this type of response, the stuporous patients, whose attention was least evident, showing the highest percentage of patterned responses and the subjects with the relatively benign condition psychoneurosis and the nonpsychotic patients, whose consciousness was quite clear, showing none. The A type of response, as indicated in table 2, appears to indicate a greater degree of disorganization than the B type, and the B type, a greater degree than the C type.

USE OF THE TEST FOR DETERMINING MENTAL EFFICIENCY IN PSYCHIATRIC DISORDERS

Method of Study.—The test was administered to 580 patients suffering from a variety of psychiatric disorders, representing almost every known form of psychosis. Nine hundred responses were obtained, many of the patients having been examined in different phases of their illness. It was found of greater importance to classify the responses according to the syndrome the patient presented than according to the formal nosologic group. Therefore the disorders with a similar clinical picture were classed together rather than those with a common etiologic or pathologic factor. Thus, alcoholic psychoses were placed with the confusional or the deteriorated syndrome, according to the clinical condition of the patient at the time of examination. In this way schizophrenia was divided into the paranoid, the confusional and the stuporous types, and a different category was formed for the chronic, static, so-called "deteriorated" type. The deterioration syndrome was reserved for the more or less irreversible psychoses showing organic-structural change. The responses were therefore classified according to the cross sectional picture of the behavior and mentation of the patient. For purposes of analysis they were divided into four groups.

Types of Responses.—GROUP 1: Incorrect Responses: Including the failures to respond and the patterned responses, 84 per cent of the total of 900 responses were incorrect. The mean error was calculated from the patterned, correct and incorrect groups, the cases in which the subject was unable to respond being excluded. The mean error scores for the various syndromes are shown in figure 2.

GROUP 2: Patterned Responses: These occurred in 139, or 15.5 per cent, of the total number of responses. The four types represented are shown in table 2, with the corresponding error score for each type. Those syndromes showing the greatest amount of disorganization, such

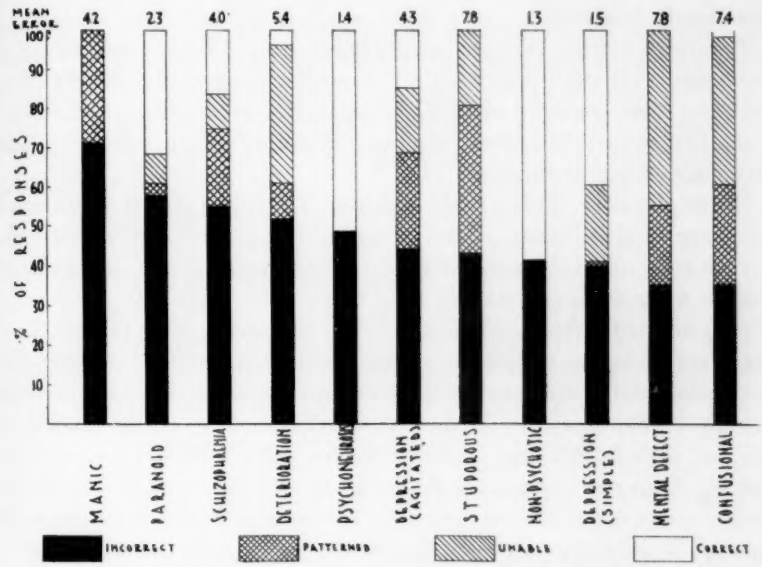

Fig. 2.—Analysis of 900 responses to the serial 7 test.

as the confusional and the stuporous, had the greatest percentage of patterned responses.

GROUP 3: Inability to Respond: Eighteen and a half per cent of the patients were unable to give any type of response. The most important factors militating against the performance of the test were severe deterioration, attention defects and negativism. Other symptoms precluding an answer were mutism, profound agitation, apathy, stupor, blocking and delirium. Such failures were, however, not consistent, and the patients might at different phases of their illness give patterned responses and in convalescence even answer the problem correctly.

GROUP 4: Correct Responses: Sixteen per cent of the total number of responses were correct. As might be expected, these occurred for

the most part in the psychoneurotic patients and the nonpsychotic subjects, who were the best preserved intellectually and showed the least disorganization.

Results in Terms of Psychiatric Syndromes.—A comprehensive diagram of the results obtained is given in figure 2. The most characteristic features of responses associated with each syndrome are given in the following descriptions.

Manic States: None of the responses of subjects with this syndrome were correct, and they showed a high proportion of patterned types. The perseveration and clang associations so characteristic a feature of the manic flight of ideas are important factors in the frequency of patterned responses in this group.

Paranoid States: This group included patients with paranoid conditions and a few well preserved schizophrenic patients whose prominent symptoms were paranoid in type. Their better preservation is indicated by the low mean error, few patterned responses and a relatively large percentage of correct answers.

Schizophrenia: This group consisted of patients with the chronic static type of the disease. They were all in the admission service, and their illness could be graded as mild to moderately severe, in few cases being in a far advanced stage.

Deteriorated States: This syndrome included the psychoses associated with organic-structural change. It was further divided into alcoholism (4.3), epilepsy (2.8), dementia paralytica (6.3), arteriosclerosis (5.2), senile (6.0) and a miscellaneous group of conditions, including encephalitis and Huntington's chorea (5.4). The mean error score for the serial 7 test for each diagnostic class is given in parentheses. The low mean error score for epilepsy is interesting in view of the recent paper by Collins, Atwell and Moore,[11] which stated that, contrary to prevailing opinion, epileptic patients are able to handle abstract concepts fairly well. To indicate the effect of severity of deterioration on the type of response, 172 responses were obtained from three groups of deteriorated patients with progressively severe disease (fig. 3). A progressive increase in the failure to respond, patterned responses and mean error scores paralleling the severity of the clinical picture can be noted. The inference might be drawn that the process of disorganization first produces errors in the test replies and that with increasing severity it may result in a patterned response and finally precludes a response entirely.

Psychoneurosis: As might be expected, the group with psychoneurosis showed a low mean error, no patterned responses and a fairly

11. Collins, A. L.; Atwell, C. R., and Moore, M.: Stanford-Binet Response Patterns in Epileptics, Am. J. Orthopsychiat. **8**:51, 1941.

high proportion of correct responses. It was apparent, however, that tension and anxiety in this condition, as well as in the more malignant disorders, had a definite effect on the production of errors.

Depressive States, Simple: It was found that the responses of patients with simple and those of patients with agitated depressions could not be included together, and it will be noted that the configuration of the bars is quite different. The addition of agitation to the picture considerably decreased the efficiency in the performance of the test.

Stuporous States: This group included schizophrenic patients mainly, with a few with depressive stupors. Most were not too mute, retarded or blocked to give some type of response. They showed a high number of patterned responses and mean error, and none gave a correct response.

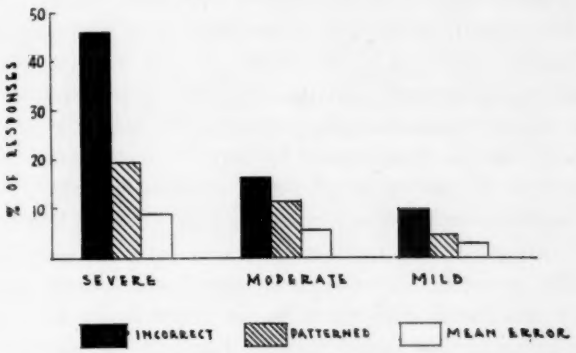

Fig. 3.—Responses of the deterioration syndrome to the serial 7 test.

Nonpsychotic States: Included in this group were patients with psychopathic personality, chronic alcoholism and simple adult maladjustment. They had the lowest mean error and the greatest number of correct responses, none showing severe enough disorganization to give a patterned response.

Depressive States, Agitated: The configuration of the bar for the group with agitated depressions should be compared with that for the subjects with simple depressions. The mean error is much higher, the patterned responses much more frequent and the correct responses considerably reduced.

Mental Deficiency: For subjects in this group the mean error and the number of patterned responses were high, and none of the answers were correct. They have been unable to form the arithmetical concepts necessary for the performance of the test and in this respect are similar to school children in the lower age groups.

Confusional States: This group included patients with schizophrenia (7.9), arteriosclerosis (5.5), dementia paralytica (9.8), alcoholism (9.0) and epilepsy (4.6), the mean error score being indicated in parentheses. Those patients were included who showed clouding of consciousness, disorientation and confusion and were for the most part acutely psychotic.

COMMENT

There are several advantages in the use of serial subtraction of 7 from 100 as a test of mental impairment. The rapidity of application and the ease of administration, obviating the necessity for special psychologic technics, makes it invaluable in routine psychiatric examinations. It has recently proved its value in this respect in the examination of Selective Service candidates, in which a rapid estimate of the intellectual resources of the subject is necessary. In many cases it has indicated the necessity for more intensive study and subsequent disqualification. It may be repeated at frequent intervals, and if memorizing is suspected one need merely change the minuend to 99 or 98. Seven was found to be the most satisfactory subtrahend and the one least likely to form patterns which might result in automatically correct answers. It is also of some prognostic aid. It has been found in certain cases that with clinical improvement the A type of response is replaced by the B type and finally in convalescence a correct response may ensue. During periods of clinical improvement the number of errors progressively diminishes, and, conversely, as retrogression occurs errors become more frequent and more grossly inaccurate and there is an increase in the number of patterned responses. No differentiation between the organic and the functional psychoses could be derived from the test results, either quantitatively or qualitatively, and a measure only of the degree of disorganization can be obtained. The importance of emotional factors on the production of errors should be emphasized. Essentially the test is a measure of mental efficiency, and not mental capacity, and any factors interfering with this efficiency, such as depression, apathy or excitement, will be reflected in the responses.

SUMMARY

A simple two minute clinical test for the measurement of mental impairment is described. The test, consisting of the serial subtraction of 7 from 100, was standardized for mental age on a group of 433 normal persons. Nine hundred responses from 580 patients with a wide variety of psychiatric disorders were analyzed. Its advantages as a quickly applicable and reasonably accurate test for intellectual efficiency are emphasized.

The Compton Sanitarium.

Case Reports

PRIMARY DEGENERATION OF THE CORPUS CALLOSUM (MARCHIAFAVA'S DISEASE)

Report of the Second American Case

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The problem of selective degeneration of single organs or parts of organs is increasingly occupying the attention of physicians. To an ever greater extent these lesions are being traced to the activity of chemical substances or to deficiencies of specific chemical substances (vitamins). Wherever they occur, whether in the liver, the bone marrow, the adrenal gland or the nervous system, they show certain features in common. Although the substance thought to be responsible may be in common use, only very few persons react unfavorably to it, and when a person does react in this way it may be to relatively small doses. The same individuality is seen in reactions to deficiencies of specific chemical substances. A constitutional factor is often further manifest in the form of familial or racial distribution of cases. The repeated use of the drug over a relatively long period seems to enhance the activity. Substances chemically or pharmacologically related may elicit similar effects. The first reports indicate great rarity of the effect, while subsequent studies show that minor degrees of the effect are much more common and the original racial distribution less constant.

Degenerative phenomena in the brain due to chemical substances often show great selectivity. Carbon monoxide, for instance, picks out the basal ganglia for its major disturbances. Associated with chronic alcoholism, several different sites of election are known, each leading to a distinct clinical syndrome. Wernicke's superior polioencephalitis is such a condition. Another is the rare primary degeneration of the corpus callosum herein described, which was first reported by Marchiafava and Bignami in 1903.[1] Since this time some 42 cases have been reported and summarized in the Italian literature. Outside of Italy only 1 case has been described—that of an Italian man in Boston.[2]

REPORT OF CASE

A married man aged 67 was admitted to the hospital in coma of about one week's duration, the coma having developed gradually until he could no longer be aroused. About three weeks before this time the patient's wife first noted marked personality changes. His memory became poor; he was confused and

1. Marchiafava, E., and Bignami, A.: Sopra un alterazione del corpo calloso osservata in soggetti alcoolisti, Riv. di pat. nerv. **8**:544, 1903.

2. King, L. S., and Meehan, M. C.: Primary Degeneration of the Corpus Callosum (Marchiafava's Disease), Arch. Neurol. & Psychiat. **36**:547 (Sept.) 1936. This paper contains a complete review of the reported cases. No attempt will therefore be made to review all the cases in my report.

often drowsy. He appeared to be looking for something all the time. Although previously of relatively stable temperament, he now easily became angry at his family, something he rarely ever did before. He would not tolerate the dog which he previously had loved. All these symptoms became more and more marked and were accompanied by weakness, which progressed until he was unable to do anything for himself. Finally he lapsed into coma, from which at first he could be aroused but which at the time of admission seemed to be complete.

The patient was born in the United States of Swiss parentage. His family knew of no definite Italian ancestry. He was a grocer and had worked hard all his life. Periodically he went on alcoholic sprees and in between times drank more than moderately.

Examination at the time of his entrance showed the patient's face to be somewhat flushed. The right pupil was slightly larger than the left, but both reacted well to light. The fundi, and especially the disks, were blurred. The patellar reflexes were absent; the biceps reflexes were present but weak. There were no abnormal reflexes. There was a large left inguinal hernia.

The patient died within forty-eight hours after his entrance, without arousing. His temperature, 99 F. on admission, rose steadily to 102.4 F. Laboratory examinations disclosed nothing significant. Spinal puncture was not performed. The clinical

Fig. 1.—The corpus callosum, natural size. The shaded areas were grossly softened and somewhat grayer than the surrounding tissue. *G* indicates the genu; *S*, the splenium.

diagnosis was probable brain tumor, and because of the marked personality changes and the absence of localizing signs, the tumor was thought to be in the frontal lobe.

Necropsy showed the immediate cause of death to be confluent bronchopneumonia in the lower lobe of the left lung. The only other gross change of note was marked hypertrophy of the gastric mucosa, which was thrown into deep rugae and histologically showed marked infiltration with lymphoid cells.

The brain weighed 1,150 Gm. The meninges were smooth. The sulci in the frontoparietal regions were slightly deeper than normal. There was no pressure furrow over the cerebellum. The ventricles showed no gross abnormality.

When the brain was sectioned the corpus callosum was found to be larger than usual (fig. 1). Both in the genu and in the splenium there were areas of soft, almost gelatinous tissue, sharply demarcated from a thin zone of apparently normal tissue which covered the softened areas dorsally and ventrally. From the genu there extended backward a zone of softened tissue less sharply demarcated and gradually thinning out posteriorly, but becoming thicker again and more prominent in the splenium. Laterally the areas of softening extended toward the hippocampus, and there were symmetric areas of softening in the corona radiata dorsolateral to the genu of the corpus callosum.

Sections of the softened area showed extensive demyelination. The junction with normal myelinated fibers was, in most places, very sharp (fig. 2 *A*), but in

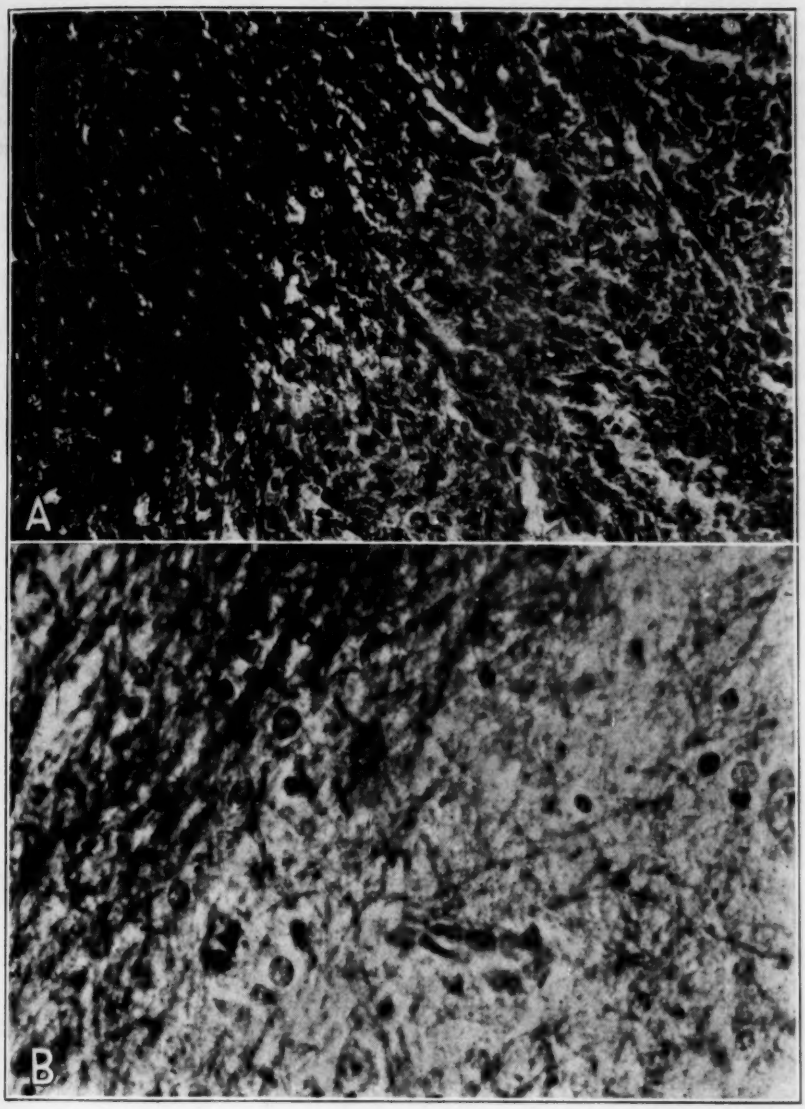

Fig. 2.—*A*, the sharp margin of a degenerated area; *B*, a few intact myelin fibers in the periphery of a degenerated area. Weil stain.

a few places a few myelinated fibers extended for variable distances into the softened areas (fig. 2 *B*). The axons were reduced in number, but many were still present (fig. 3). Some of them showed clubbing and fragmentation.

Throughout most of the softened area, but most pronounced near the periphery, there were large numbers of gitter cells (fig. 4) crowded with lipoid. No blood pigment could be seen in most of the tissue even after special stains for iron. The capillaries and smaller arterioles were markedly proliferated. Budding of capillaries was seen in many areas. The reticulin fibers about the arterioles and capillaries were increased in amount, and small fibrils extended into the zone of gitter cells.

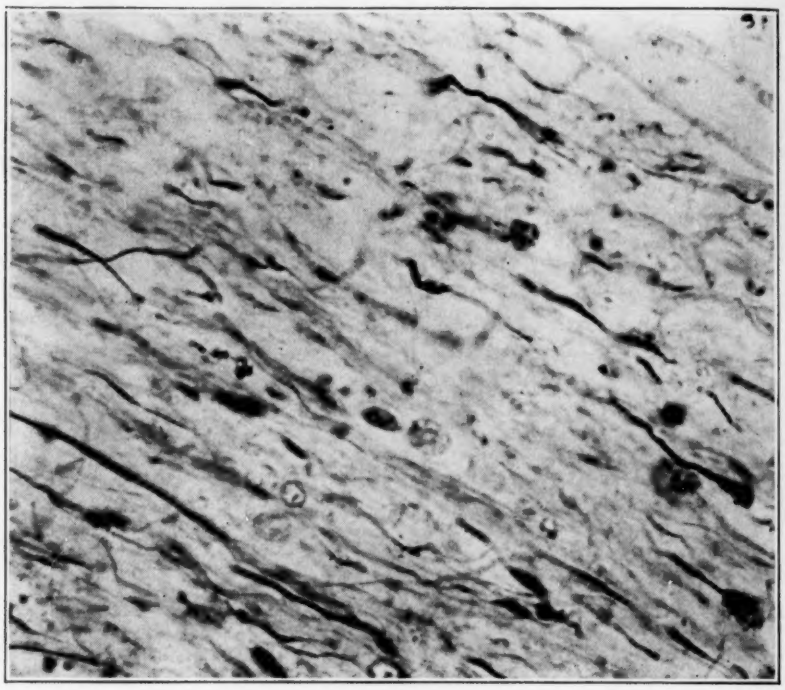

Fig. 3.—Preserved axons within the demyelinated area, showing some clubbing and fragmentation. Davenport stain.

Search through many sections showed about a half-dozen microscopic areas of hemorrhage (fig. 5). The red cells were, for the most part, intact, but small amounts of hemosiderin could be found. A few tiny areas of necrosis were also seen, and occasionally the hemorrhage surrounded an area of necrosis.

The histologic changes in the corpus callosum and in the corona radiata were identical. Careful search of the frontal, parietal and occipital cortex and subcortex, the basal ganglia, the mamillary bodies, the hippocampus, the optic nerves and the optic chiasm failed to reveal necrosis or demyelination. The vascularity of the subcortical gray matter was somewhat greater than usual.

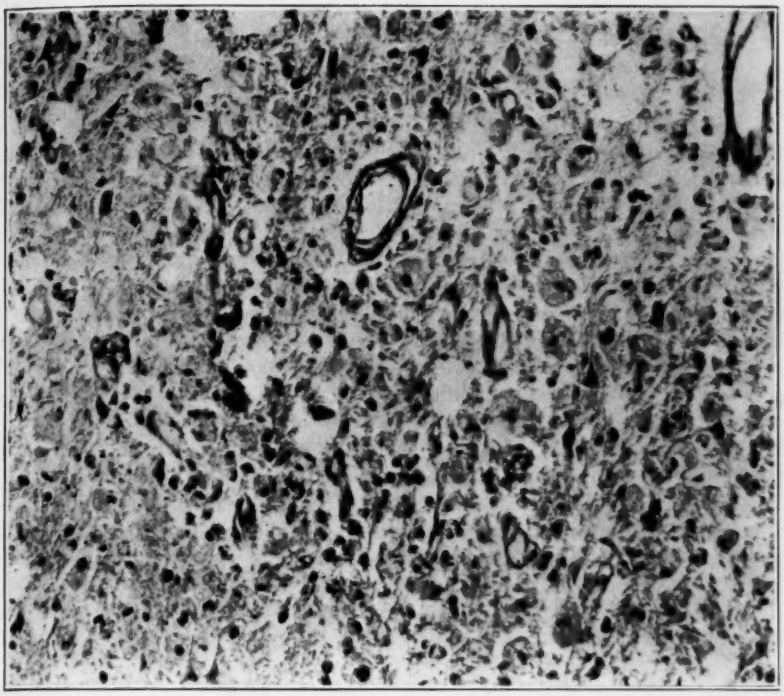

Fig. 4.—Increased vascularity and many gitter cells. Hematoxylin and eosin stain.

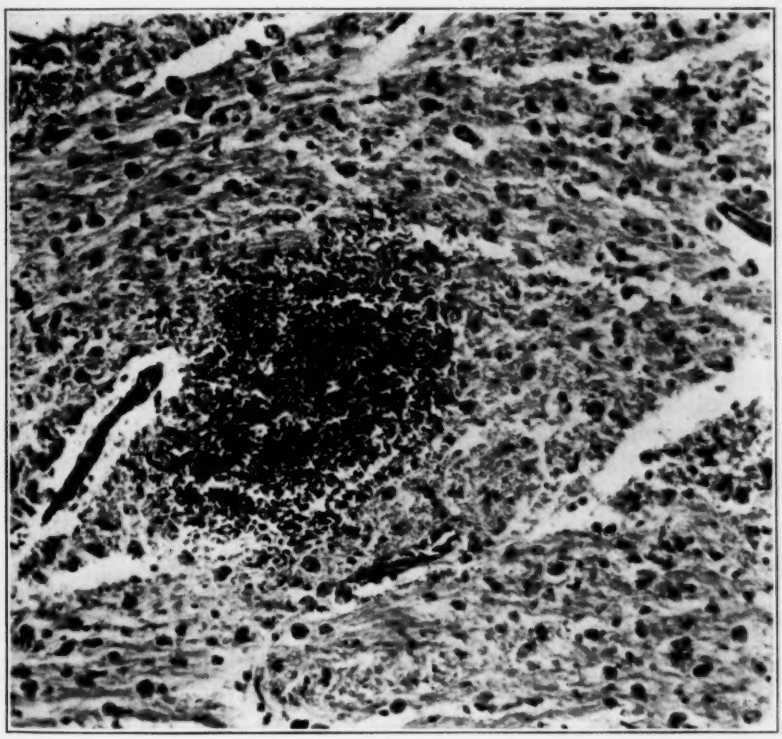

Fig. 5.—Area of recent hemorrhage. Hematoxylin and eosin stain.

COMMENT

The clinical syndrome in the reported cases of primary degeneration of the corpus callosum is a very constant one, consisting of a variable period (weeks or months) of mental changes, especially those collectively known as "personality changes," followed by apoplectiform or epileptiform seizures and, finally, by coma. That the antemortem diagnosis has never been made is explainable by the extreme rarity of the cases so far described and by the fact that better known pathologic states may produce the same symptoms. The most commonly made diagnosis is that of tumor of the frontal lobe. Since tumors and cysts of the corpus callosum also lead to a diagnosis of changes in the frontal lobe, it may be inferred that the psychic changes at least are due to the site of the lesion. Connections between the corpus callosum and the neocortex have been described.[3] A second important set of connections is with the hippocampus, also a region which participates in psychic functions.

Pathologically the lesions also show marked constancy. The gross changes consist of softening in a middle lamina of the corpus callosum, leaving a zone of normal tissue both dorsal and ventral to the involved area. The genu is nearly always involved, the splenium often, and the intermediate tissue to a variable extent, but always only in the midzone. In the midline there may be an area of unaltered tissue, leaving symmetric areas of softening extending to the lateral limits of the corpus callosum. The areas of softening are gray and very friable (it is difficult to cut frozen sections, and artefactitious clefts occur in paraffin-embedded tissue). Hemorrhagic areas are not reported. It must be mentioned that the constancy of these lesions may be due to the fact that slighter degrees of involvement and variants have so far escaped observation.

Lesions resembling those in the corpus callosum may, in addition, be found in other sites. The one most commonly described is in the corona radiata just dorsolateral to the genu; this was the only extracallosal area of involvement observed in the present case. The centrum ovale and the brachium pontis have also been described as participating in the degeneration. King and Meehan reported demyelination in the optic chiasm, and in a personal communication King mentioned that he is particularly interested in this feature. I did not find changes in the optic tract in my case.

The histologic changes are essentially those of extensive demyelination with relative preservation of the axons. The other changes may all be explained as reactive to this process. There is marked proliferation of phagocytic glia elements (gitter cells), containing lipoid. The small arterioles and capillaries show active proliferation, although not always to the marked degree found in King's case. There is not the slightest evidence of inflammatory reaction in the usual meaning of the term. Small foci of hemorrhage and necrosis, such as were seen in the present case, have not been described before. It is unlikely, however, that this is evidence that the earliest lesion is an extensive necrosis. The slow evolution of symptoms, the absence of blood pigment and the

3. Tilney, F.: The Hippocampus and Its Relations to the Corpus Callosum, J. Nerv. & Ment. Dis. **89**:433, 1939.

presence of axis-cylinders all favor the assumption that the lesion develops too slowly to be a hemorrhagic necrosis.

The lesion described in the cases in man has been reproduced in all its gross and histologic characteristics by the long-continued injections of sublethal doses of potassium cyanide into cats [4]: elective localization in the corpus callosum, involvement of only the middle lamina, demyelination and preservation of the axons. The lesions could not be produced in rats, rabbits or guinea pigs, and in dogs the site of election was the globus pallidus and the substantia nigra. The species specificity following the use of the same chemical substance indicates the importance of the constitutional factor in determining the reaction to a drug or to a vitamin deficiency.

The histologic and some of the gross features are characteristic of a large number of degenerations in the central nervous system, which vary principally in the site. Accompanied by infiltration of hematogenous cells, these same changes are also seen in inflammations, and when the inflammatory changes have receded the degenerative changes may closely resemble those seen in the primary degenerations. In a recent case of anterior poliomyelitis, for instance, in which death occurred two weeks after the onset, there were found a few areas, located in the anterior horns of the spinal cord and in the pons, indistinguishable from those observed in the present case. Other types of primary degeneration in various parts of the brain due to a variety of toxic agents show different gross and histologic features. At one end of the scale acute necrosis and hemorrhage are seen, and at the other, extensive gliosis. It is probable that this variability is a function of the rate of degeneration rather than of the specific etiologic agent. The influence of the tempo of change on the histologic features of a pathologic process is seen in a variety of conditions: in inflammations and neoplasms, as well as in degeneration. In the liver, for instance, acute necrosis (acute yellow atrophy) occurs if the toxic agent is present in large amounts or if the tissue is especially susceptible, while slower degeneration is accompanied by proliferation and presents the picture of subacute atrophy. The slowest rate of degeneration leads to extensive fibrosis.

Perhaps the two most striking etiologic factors in primary degeneration of the corpus callosum are the influence of alcohol and the racial history.

Alcoholism has been considered the causative agent in most of the reported cases. Only in the case of King and Meehan was there no history of alcoholism. Chronic alcoholism is also a prominent feature in the history in cases of Wernicke's disease.[5] This syndrome is usually associated with somewhat more rapid demyelination than is seen in Marchiafava's disease, and necrosis and hemorrhage may be outstanding. In spite of the name hemorrhagic necrosis, so often applied to the con-

4. Jervis, G.: Sulle alterazioni mieliniche da cinauro, Riv. di pat. nerv. **50**:410, 1937.

5. (*a*) Campbell, A. C. P., and Biggart, J. H.: Wernicke's Encephalopathy (Polioencephalitis Haemorrhagica Superior): Its Alcoholic and Non-Alcoholic Incidence, J. Path. & Bact. **48**:245, 1939. (*b*) Vonderahe, A. R.: Sequelae of Severe Disease of the Abdominal Viscera, J. A. M. A. **116**:390 (Feb. 1) 1941.

dition, these features are not shown in all cases, and changes comparable to those seen histologically in primary degeneration of the corpus callosum are not uncommonly found. A considerable number of instances of Wernicke's encephalitis have been described in which a history of alcoholism could not be obtained.[5]

Recent work in several different fields has indicated that when the same pathologic state is observed commonly in persons with chronic alcoholism and, less commonly, in nonalcoholic persons a common denominator may be found in vitamin deficiency.[6] The recent experimental work of György and Goldblatt [7] indicates the possibility that even cirrhosis of the liver may be related to deficiency of vitamin G (B_2). Ecker and Woltman [8] after the study of a case of the disease in a nonalcoholic woman enunciated the hypothesis that Wernicke's disease is caused by a vitamin B deficiency. The mechanism by which the vitamin deficiency is induced is not so much a deficiency in the intake with the diet as an inability for one reason or another to absorb the vitamin. In my case the chronic hypertrophic gastritis could well have led to the deficient absorption of vitamin B. As a matter of fact, gastric disease is responsible for most of the cases of Wernicke's disease without a history of alcoholism.[5b]

The role of vitamin B deficiency in the production of degenerative lesions in the central and peripheral nervous system is not limited to those resulting from chronic alcoholism. The changes in the cord of pernicious anemia, the peripheral neuritis associated with a variety of toxic states and metabolic disturbances and the demyelination in both the brain and the peripheral nerves in experimental vitamin B_1 deficiencies [9] all point to the importance of substances of the vitamin B complex in the maintenance of an intact nervous system. It is probable, from both clinical and experimental data, that thiamine (vitamin B_1) is the most important for its effects on the nervous system of the group of substances making up the vitamin B complex,[10] but since it is difficult, at least in clinical studies, to separate one constituent of the complex from the others, thiamine may not be the only factor of significance.

If it is true that the degenerative phenomena in the case are caused by a deficiency of thiamine and the histologic characteristics of the degeneration are determined by the tempo of the change, there is left to be explained only the selective localization of the pathologic process. It is here, perhaps, that the second great peculiarity of the disease, the racial incidence, is of importance.

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6. Stevenson, L. D.: A Study of the Changes in the Brain in Alcoholism, Arch. Path. **30**:642 (Aug.) 1940.

7. György, P., and Goldblatt, H.: Hepatic Injury on a Nutritional Basis in Rats, J. Exper. Med. **70**:185, 1939.

8. Ecker, A. D., and Woltman, H. W.: Is Nutritional Deficiency Basis of Wernicke's Disease? Report of a Case, J. A. M. A. **112**:1794 (May 6) 1939.

9. Alexander, L.: Wernicke's Disease: Identity of Lesions Produced Experimentally by B_1 Avitaminosis in Pigeons with Hemorrhagic Polioencephalitis Occurring in Chronic Alcoholism in Man, Am. J. Path. **16**:61, 1940.

10. Wolbach, S. B.: Central Nervous System Changes in Vitamin Deficiency States, Arch. Path. **30**:627 (Aug.) 1940.

Of the 43 cases described, 41 have occurred in Italy and 2 in the United States. Of the latter, the first was that of an Italian in Boston, and the second, the present case, that of a man of Swiss ancestry. With regard to the latter, it must be remembered that there has always been considerable infiltration of Italians into Switzerland and that Italian is one of the commonly used languages in that country. King and Meehan made the point that other conditions, such as Buerger's disease, have been thought at one time to occur exclusively in a single race and have been found later in people of other races. That is undoubtedly true, and Marchiafava's disease may soon be described in non-Italians.

Is this a racial disease? Such a question is not always easy to answer. Custom, geographic influences and other factors may lead to racial distribution.[11] If by a racial disease one means merely that it is more common or is almost exclusively found in a single race regardless of the reason, the significance of the racial factor may not be the same as if one means that genetic differences in the race are a factor. So small a number of cases as that of the disease now under discussion cannot, of course, lead to a decisive answer concerning the importance of race for Marchiafava's disease. There is, however, a strong probability that a constitutional factor is of considerable significance. Since thiamine deficiency is probably responsible for degenerations in the nervous system in many different sites, in which no particular racial tendency is shown, while the changes in the corpus callosum show the racial tendency to so marked a degree, it is probable that the constitutional factor is responsible for the elective localization of the degenerative process in the corpus callosum. It will be remembered that in the experimental reproduction of callosal degeneration species differences were observed [4] both in determining whether or not degeneration would occur and in the site of the degeneration.

SUMMARY

This report on primary degeneration of the corpus callosum (Marchiafava's disease) records the forty-third case in the medical literature and the second in the United States, all the other cases having been reported from Italy. The patient was of Swiss ancestry and, like the great majority of similarly affected persons, was a chronic alcohol addict.

The essential pathologic process was one of demyelination with reactive proliferation of phagocytic glia cells and blood vessels.

It is suggested that, in common with Wernicke's hemorrhagic encephalitis and other degenerations of the nervous system associated with alcoholism and other toxic agents, the essential etiologic moment is a deficiency of a member of the vitamin B complex, probably of that constituent known as vitamin B_1, or thiamine.

In common with other degenerative processes, a constitutional factor is of marked importance. The racial factor so consistent in this disease may determine the site of degeneration in the corpus callosum.

420 Lincoln Road.

11. Bohrod, M. G.: Keloids and Sexual Selection: A Study in the Racial Distribution of Disease, Arch. Dermat. & Syph. **36**:19 (July) 1937.

SPINA BIFIDA WITH MENINGOCELE

Occurrence in Two Children of the Same Family

BERNARD HAROLD SHULMAN, M.D., BROOKLYN

We are reporting the occurrence of spina bifida cystica with meningocele in 2 successive siblings of the same family. Such familial repetition is unusual. According to Bucy,[1] the cystic form of spina bifida occurs about once in every thousand births. The cases forming the basis of his report occurred singly in families. Woltman[2] found that in 2 of 187 cases there was definite or presumptive evidence of spina bifida in other members of the same family. In 3 of Cutler's[3] series of 62 cases of spina bifida with cephalocele there was a postive history of spina bifida or hydrocephalus in other siblings. Sachs,[4] in his discussion of congenital anomalies of the nervous system, referred to a family in which 3 successive children had spina bifida. Murphy,[5] in his excellent survey, reported 4 cases of recurrent familial spina bifida. Earlier reports of the presence of spina bifida cystica in more than one member of a family were made by Butler-Smythe,[6] Wright[7] and Pendleton.[8]

REPORT OF CASES

CASE 1.—J. B., a 2½ year old white girl, was admitted to Kings County Hospital in August 1940, because of progressive enlargement of the head and recent onset of fever.

Family History.—Both parents were in good health. There was no history of syphilis. There was, likewise, no history of spina bifida or other anomalies

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From the Department of Pediatrics, Long Island Division, Kings County Hospital.

1. Bucy, P. C.: Spina Bifida and Associated Malformations, in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1936, vol. 4, chap. 15, p. 4..

2. Woltman, H. W.: Spina Bifida: Review of One Hundred and Eighty-Seven Cases, Minnesota Med. **4**:244, 1921.

3. Cutler, G. D.: End Results in Sixty-Two Cases of Spina Bifida and Cephalocele, Arch. Neurol. & Psychiat. **12**:149 (Aug.) 1924.

4. Sachs, E.: Surgery of the Head and Spine, in Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1925, vol. 7, chap. 159, p. 93.

5. Murphy, D. F.: Congenital Malformation, Philadelphia, University of Pennsylvania Press, 1940.

6. Butler-Smythe, A. C.: Spina Bifida and Hydrocephalus Occurring in the Same Family, Lancet **1**:272, 1889.

7. Wright, H. A.: Twins, Each with Syringo-Myelocele, Canad. Prac. & Rev. **25**:205, 1899.

8. Pendleton, E. M.: Spina Bifida: Three Cases from One Mother, South. M. & S. J. **13**:215, 1857.

in the family. One brother died at the age of 9 years of heart trouble, and 1 was well at 10 years of age.

The patient was born spontaneously at term, after a labor of six and one-half hours. At birth spina bifida was present over the lumbosacral region, with a large sac, containing blood-stained fluid, protruding from the defect. There were associated flaccidity of the lower extremities and a mongoloid aspect to the features of the face. Roentgenograms taken shortly after birth revealed a soft tissue mass, compatible with the presence of a meningocele, extending from the twelfth thoracic to the fourth lumbar vertebra.

The infant was discharged from the hospital approximately two weeks after birth. For the ensuing two years the child was cared for at home. Shortly after discharge the parents noted that the head was gradually increasing in size. The child was never able to use the lower extremities or hold her head up unassisted. For the last year and a half she had required daily enemas. During this period the meningocele drained spinal fluid, which necessitated daily sterile dressings. Shortly before the last admission the child began to have a low grade fever, and for this reason she was hospitalized.

On admission, the child appeared well nourished, though obviously poorly developed. The temperature was 100.8 F. The head was large, measuring 57 cm. in circumference. The anterior fontanel was open and bulging. Fundoscopic examination revealed bilateral optic nerve atrophy. A large, irregular cystic mass protruded from the lumbar region of the back. There was associated flaccid paralysis with marked wasting.

Soon after admission the temperature rose to 104 F.; the child became comatose and died two days later. The cause of death was sepsis, with probable meningitis. Necropsy was not performed.

CASE 2.—A brother, W. B., was born spontaneously at term. It was noticed at delivery that a large meningocele was present in the lumbosacral area. This cystic mass measured 13 by 15 cm. The circumference of the head at the same time measured 31.5 cm.

Laboratory Data.—The Wassermann reaction of the blood was negative. The blood count revealed leukocytosis, with a count of 22,000 and an increased polymorphonuclear ratio, a red cell count of 6,000,000 and a hemoglobin concentration of 110 per cent (Sahli). The results of urinalysis were normal. The calcium phosphorus and phosphatase of the blood were within normal limits. Examination of the spinal fluid showed only a trace of sugar and no detectable protein with use of the Pandy reagent. No cells were present. Quantitative estimation of the spinal fluid showed a protein content of 172 mg. and a chloride level of 564 mg. per hundred cubic centimeters.

Roentgenograms of the spine disclosed evidence of a large soft tissue shadow over the lower lumbar vertebrae.

The infant was transferred from the newborn infants' nursery to the pediatric service. Twelve days after birth complete paralysis of the lower limbs was observed for the first time. Evidence of the rapidly progressing hydrocephalus was manifested by enlargement of the skull, separation of the sutures, bulging of the anterior and posterior fontanels and dilatation of the superficial veins of the scalp. The meningocele began to drain after the first week and soon became grossly infected. One month after admission meningitis developed and the infant died.

Autopsy.—The primary gross observations were: spina bifida with meningocele of the lumbosacral area; meningitis of the spinal cord and brain; internal hydrocephalus, and bronchopneumonia.

Central Nervous System: The meninges over the cerebrum and cerebellum were smooth and glistening, while those covering the base of the brain and the medulla were dull and showed a thick white exudate beneath. The convolutions appeared flattened. On section, the ventricles were seen to be greatly dilated and to contain a large quantity of gray purulent material. The cortex was atrophied and varied in thickness from 1 to 1.5 cm. The meningocele and lumbar portion of the cord were removed intact. The lumbar portion of the spinal cord was noted in the upper part of the meningocele. The meninges were thickened. Several large, yellowish white areas of exudate were noted in the mass. The spina bifida extended from the twelfth thoracic through the third sacral vertebra and measured 3.5 by 9.5 cm.

Roentgenograms taken of the spine of the 10 year old brother, who has been in excellent health, showed it to be normal.

CONCLUSIONS

The occurrence of spina bifida with meningocele in 2 children of the same family is reported.

Such familial repetition is unusual. However, it is a possibility which must be kept in mind, particularly when the condition has occurred once in a family and the parents desire to know the possibility of recurrence.

The Department of Pathology of the Long Island College Division at Kings County Hospital supplied the autopsy material.

News and Comment

AMERICAN BOARD OF NEUROLOGICAL SURGERY

The next examination of the American Board of Neurological Surgery will be held on May 12 and 13, 1942 at the Neurological Institute in New York.

SCHEDULES FOR CIVILIAN DEFENSE WORKERS

A series of training schedules for the instruction of civilian defense workers in the basic facts concerning the behavior of people under stress has been drawn up by the Committee of Military Mobilization of the American Psychiatric Association. Schedules dealing with morale, fatigue and anxiety are available. Copies may be obtained without cost from Dr. D. Ewen Cameron, Albany Hospital, Albany, N. Y.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Psychiatry and Psychopathology

EMOTIONAL FACTOR IN BRONCHIAL ASTHMA IN CHILDREN. REYNOLD A. JENSEN and ALBERT V. STOESSER, Am. J. Dis. Child. **62**:80 (July) 1941.

Jensen and Stoesser report the cases of 4 patients between the ages of 9 and 16 years whose chief complaint was asthma. All of the 4 children were girls. All were described as highly nervous, under definite emotional tension and anxious. The authors define asthma as a "disturbance of respiration in which there is bronchiospasm and excessive secretion of mucus." They believe that psychic factors in and of themselves cannot cause asthma but that they may be significant in the disease. They emphasize the importance of recognizing and dealing with the emotional factors in all cases of asthma, but particularly those in which the disease is refractory to the usual types of therapy. They stress the fact that psychologic factors should not be dealt with as a last resort, but that one should take cognizance of their importance and deal with them early in the treatment of asthma, while treatment of the physical manifestations is in process.

WAGGONER, Ann Arbor, Mich.

THE SO-CALLED EPILEPTIC PERSONALITY AS INVESTIGATED BY THE KENT-ROSANOFF TEST. RUSSELL MEYERS and SYLVIA BRECHER, J. Abnorm. & Social Psychol. **36**:413 (July) 1941.

Meyers and Brecher tried to determine whether the responses made by epileptic patients on the Kent-Rosanoff free word association test were in any manner characteristic of these persons. This was an attempt to demonstrate the influence of the alleged "epileptic personality" on free association responses. Fifty male subjects were studied. Twenty-five of these were suffering from recurring epileptiform seizures. The control group consisted of 25 persons closely matched with the experimental subjects in respect to age, sex, educational achievement, general social and economic status and intelligence.

The Kent-Rosanoff test was administered twice to each subject, the interval between the first and the second test being approximately twenty-four hours. On retest, the order of words employed in the first test was reversed. Comparisons were made between the two groups in respect to the speed of reaction time, the numbers of common and doubtful responses, the frequency and types of individual responses, the perseverative tendencies on retest and the relation between the intelligence quotient and the number of individual responses. The results for each item of inquiry failed to disclose any significant disparities between the two groups tested. Within the limitations of the experiment the data derived fail to support the clinical concept that a specific personality syndrome characterizes the epileptic patient.

WISE, Howard, R. I.

PSYCHODYNAMISMS IN ANOREXIA NERVOSA AND NEUROTIC VOMITING. JULES H. MASSERMAN, Psychoanalyt. Quart. **10**:211, 1941.

Masserman reports on the analysis of a 35 year old woman who suffered from anorexia nervosa. The patient's difficulty was based on her deep-seated primary oral attachment to and her passive overdependence on her mother. In her childhood this attachment had been formed through the mother's attitude and the

absence of the father and had been threatened when the girl learned that it was not the mother, but an uncle, who provided for her. This knowledge had produced a severe conflict concerned with how she could divide her allegiance between her uncle and her mother without incurring the latter's jealousy. In dealing with this conflict she had used the following mechanisms: 1. Since all levels of development more mature than the primary oral attachment were dangerous, she had renounced all aggressive and genital strivings. 2. The genital renunciation had resulted in her using pregenital mechanisms, i. e., anal-sadistic depreciation of genitality, masochism and a defense of her secondary narcissism by pretending to do what her mother wanted. The overdependence on her mother resulted in a wish to be masculine, which she felt would please her mother. In order to accomplish this wish, she shifted her oral wishes from the mother to a man and had a strong unconscious wish to castrate orally any man to whom she was attracted. Because of this fantasy she felt that taking food in the presence of a man was the same as castrating him orally, and she vomited in order to deny her cannibalistic ideas and to restore the penis she had disowned in fantasy. Her vomiting therefore was (1) a symbolic rejection and restitution of the father's penis, which she had fantasied she had incorporated orally so that she could retain her mother for herself to the exclusion of any other person; (2) an aggressive attack on her thwarting parents; (3) a masochistic expiation for such an attack.

PEARSON, Philadelphia.

RORSCHACH REACTIONS IN EARLY CHILDHOOD. BRUNO KLOPFER and HELEN MARGULIES, Rorschach Research Exchange **5**:1 (Jan.) 1941.

The authors studied 205 Rorschach records of 155 children between the ages of 2 and 7 years. They found the following successive patterns:

1. The most undifferentiated reaction was a "magic repetition" of the same response to all ten cards. This reaction became rare after 3 years of age and disappeared completely when the fourth year was reached.

2. This repetition can be substituted by a rejection of cards either by silence or by a statement such as "I don't know." This was considered a typical reaction of young children only when more than three cards were so rejected.

3. In another modification of this "magic repetition" response the perseveration may be limited to some of the cards, the others being given more individual attention. Records were included in the reaction pattern if the perseveration included at least four different cards, provided the card was used as a whole.

These modifications of the earliest reaction patterns are frequent between 2 and 4 years of age, diminish between 4 and 5 years and are rare after 5 years.

A third, and decisive, step is shown when at least seven of the ten cards receive individual responses. These responses may be very crude, may have only a faint resemblance to the blot or may assign to the whole blot a meaning suggested by a minor detail only (confabulation).

None of the children studied showed this pattern before the age of 3 years, but it was present in 99 per cent of the children who were 5 to 5½ years of age and in all those over 5½ years of age.

Within this step a minor modification is the perseveration of responses to the last three cards, "where the color seems to create similar situations calling for the 'magic key solution' as the whole Rorschach situation presents at an earlier age."

In the youngest age groups (2 to 3 years) over one third of the children rejected cards and all of them except 1 rejected more than two cards. Of the 3 to 4 year age group 30 per cent rejected cards, several rejecting more than two. In the next two age groups the proportion fell to 13 and 12 per cent, and in each group only 2 children rejected more than two cards. In the last group (6 to 7 years) only 1 out of 23 children rejected three cards. In the succeeding age groups there was a steady decrease in the percentage of children who used only W

(whole card) responses, from 35 per cent in the 2 year group to none in the 6 year group. D responses (the most obvious detail areas) increased correspondingly and were found exclusively or predominantly in all but 2 cases in which details were used.

M (human movement) responses are unusual in children, and it is most likely that below the 8 year level they are found almost exclusively in the records of superior children.

FM (animal movement) responses showed a consistent rise at succeeding age levels and consistently exceeded M responses. This tends "to confirm the interpretive asumption that FM represents a symbolic expression of instinctual drives which up to puberty naturally predominate in our inner life."

Scattered samples of M (inanimate movement) responses, as well as of the six types of shading response, were seen at all levels.

Within the color responses the pure C response has a dominant position up to the age of 4 years. After this the CF (color definite, form arbitrary) response dominates to the age of 6; then the usual adult dominance of the FC (definite form and color combined) response emerges.

F (pure form) responses remained close to 50 per cent of the total in all these age groups, but the quality of the responses, or the form accuracy level, increased with age.

MARCOVITZ, Philadelphia.

PECULIAR PERSONALITIES: DISORDERS OF MOOD; PSYCHOPATHIC PERSONALITY. ROSCOE W. HALL, War Med. **1**:383 (May) 1941.

Hall believes that both the psychopathic and the manic-depressive personality should be rejected for military service. Particular attention should be paid to the presence or absence of a history of previous hospitalizations. The problem as to whether a draftee with a bad psychic heredity should be rejected should be left for the psychiatrist to decide in the individual case.

PEARSON, Philadelphia.

PSYCHOSES FROM BROMIDES. G. NIZZI NUTI, Gior. di clin. med. **21**:1451 (Dec. 10) 1940.

According to Nizzi Nuti, psychoses produced by bromides are more frequent than is generally believed. They show the acute phase of bromide intoxication. A neuropathic constitution, a diet poor in salt and a personal sensitivity to the drug are the most important predisposing factors. The diagnosis is made from the clinical history of the patient and the local and general clinical symptoms. The course and prognosis of the intoxication are, as a rule, benign. They depend on the acuteness of the intoxication and the functional condition of the kidney. The best, and most simple, treatment consists in immediate discontinuation of the drug and of any sedatives and the oral administration of 5 Gm. of sodium chloride daily for about one month. A diet rich in salt completes the treatment. During the first few days there are hyperbromidemia and aggravation of the psychosis, which improves as the treatment progresses. When there is a great amount of bromides in the blood, repeated aspiration of the gastric juice with a stomach tube at frequent intervals is advisable. Sodium chloride and food are administered by tube. Spinal fluid drainage may be resorted to in cases of acute psychosis to prevent intracranial hyperpressure. The maintenance of normal intestinal and renal function is constantly controlled. The author reports 2 instances of bromide intoxication occurring in neuropathic patients who had had a diet poor in salt and diminished chloridemia. The amount of bromides in the gastric juice was increased before treatment and diminished after it. The basal metabolism, which was increased before treatment, became normal after. The amount of chlorides in the blood slightly increased. Discontinuation of bromides and salt therapy resulted in rapid recovery of the patients.

J. A. M. A.

Meninges and Blood Vessels

LUMBAR PUNCTURE AS A FACTOR IN THE PATHOGENESIS OF MENINGITIS. LAURENCE G. PRAY, Am. J. Dis. Child. **62**:295 (Aug.) 1941.

Pray reviews the pathogenesis of meningitis, suggesting that it arises in one of three general ways: Organisms may reach the subarachnoid space by direct traumatic implantation; infection may extend to the meninges from an adjacent lesion, or organisms may reach the meninges by passing the blood-brain barrier. Because lumbar puncture entails the risk of producing meningitis, the author considers it important to determine the possible degree of danger in this procedure. For this purpose he selected 207 cases of pneumococcic meningitis. Of these, lumbar puncture was done before the onset of meningitis in 6 per cent, or 13 cases. Although he agrees that the conclusions from experimental work make it obvious that lumbar puncture may be an important factor in the production of meningitis in cases of bacteremia, he feels that it was not an important factor in the clinical cases which constitute his study. Lowering of cerebrospinal fluid pressure may produce meningitis not only by drawing organisms through the blood-brain barrier but by rupture into the subarachnoid space of a focus of infection contiguous with the meninges as a result of release of pressure. Lumbar puncture through infected tissues may introduce organisms directly into the meninges. In spite of these risks, the author believes that the necessity of arriving at a diagnosis is frequently sufficiently important to warrant making the puncture. He concludes that the material which he studied is evidence that, in general, lumbar puncture is not hazardous for the patient with bacteremia, and he bases his conclusion on the fact that the incidence of meningitis was no greater among patients with bacteremia who had lumbar puncture, with a yield of normal spinal fluid, than among those for whom no diagnostic tap was performed. In general, the author minimizes the danger of producing meningitis by the diagnostic spinal tap.

WAGGONER, Ann Arbor, Mich.

PNEUMOCOCCIC MENINGITIS. GOODLATTE B. GILMORE and PHILIP SACKS, Arch. Otolaryng. **32**:1007 (Dec.) 1940.

Sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine), the specific pneumococcus serum and adequate surgical removal of the primary focus have resulted in an increase in the number of recoveries from pneumococcic meningitis. Meningitis in the presence of an aural infection is most often secondary to an otitic lesion but may be due to sinusitis, especially sphenoiditis, or respiratory disease or may even be primary. Operation in the primary stage may prevent further advance of the disease. It is important to obtain a culture early because the sulfanilamide drugs alter the organisms, making identification and typing difficult or impossible. If a walled-off secondary focus occurs, neither the chemical nor the biologic agent will prevent death. Of all the pneumococcic infections of the meninges, that due to Pneumococcus type III is most often secondary to an otitic lesion and is most apt to terminate fatally. Of 113 cases of recoveries from pneumococcic meningitis, including the 2 reported in this article, the ear was the source in 27.5 per cent and the sinuses in 5.3 per cent. The article includes tables illustrating the primary site, the organism and the percentage of recovery for each age decade of the patients. Of the cases of otitis, in 5 a mastoidectomy was performed before the onset of meningitis and in 16 after the onset of meningitis, while in 10 no surgical treatment was given. Kreutz and Witter reported that of 300 cases of acute mastoiditis in which cultures were made at operation pneumococci were revealed in 20. In 16 of these the organism was of type III. Of these 16, death occurred in 8, making a mortality of 50 per cent. Sulfapyridine has been shown experimentally to cause the pneumococcus to lose its capsule. The bacteria may develop tolerance to the drug. Apparently the different strains vary in sensitivity, according to MacLean, Rogers and Fleming, who suggested that since the chemical is bacteriostatic only

a specific antibacterial serum or vaccine should be used. Bullowa reported that of patients with pneumonia treated with serum in the first four days 12.3 per cent died, of those treated with sulfapyridine 9.4 per cent died and of those treated with serum and sulfapyridine 2.6 per cent died. The antibodies, present in the blood normally or acquired as a result of vaccination or disease, do not enter the cerebrospinal fluid through the choroid plexus or the meninges if these structures are intact. In meningitis, however, a small amount of immune bodies can enter the cerebrospinal fluid. Since antibodies have slight permeability through the meningovascular barrier and because the patient's own serum is less likely to cause an untoward reaction, Finland, Brown and Raugh administered the patient's serum intrathecally soon after the intravenous use of specific pneumococcus serum. The absorption of sulfapyridine from the gastrointestinal tract being irregular and limited, administration of the drug should be supplemented by the use of sulfapyridine sodium intravenously, to maintain the concentration of the drug in the tissues at the desired level. Experimental data and clinical observation emphasize the importance of augmenting the patient's immunity when sulfapyridine is given, so that the invading cocci may be destroyed before there has been time for tolerance to the drug to develop. Furthermore, by the combined use of the drug and serum the doses of both may possibly be reduced, with lessening of toxic effects. Blood transfusions from immunized, compatible, convalescent donors should be made. Ample fluid intake and sufficient sodium chloride lessen the tendency to block, which is apt to occur in cases of pneumococcic meningitis. Some advocate no surgical intervention in cases of infection of the cerebrospinal system. The results of chemotherapy have to a degree supported such contentions. Certainly, it is an advantage to saturate the blood with the sulfanilamide drugs before attacking the primary focus. The masking effects must then be kept well in mind. It would seem safer to operate in the presence of meningitis if there is any doubt. Meningitis following mastoidectomy may possibly be due to a breaking down of inflammatory barriers. However, when a meningeal infection occurs before mastoidectomy is performed the barriers no longer act as a safeguard. The primary focus now acts as a base, and immediate complete operation is indicated. The 111 cases of pneumococcus type III meningitis with recovery recorded to date in the English literature are reviewed in a table, together with 2 cases of the authors, in 1 of which, the first of its kind to be reported, the causative organism was the type XVIII pneumococcus. Since the paper was written, 3 cases of otitic pneumococcic meningitis, due to type XVIII, IV and III, have been reported, in addition to 6 other cases of nonotitic origin.

HUNTER, Philadelphia.

OTITIC MENINGITIS DUE TO BACILLUS PROTEUS. NELSON R. CRAGG, Arch. Otolaryng. **34**:345 (Aug.) 1941.

Bacillus proteus has rarely been found to be a cause of meningitis. Cragg reports the case of a girl who was admitted to the hospital with mastoiditis on the left side and symptoms of intracranial involvement. The white blood cells numbered 18,000; the spinal fluid was cloudy, and a smear showed a gram-negative rod. Shortly after admission to the hospital a modified radical mastoidectomy was done, revealing a perisinal abscess and the lateral sinus covered with granulations. Sulfanilamide was given. B. proteus was found in the cultures of the blood, the spinal fluid and material from the external ear and the mastoid wound. The internal jugular vein was then ligated, after which palsy of the seventh and sixth nerves developed; the petrous tip was explored, with negative results. The patient improved, and after seven days treatment with sulfanilamide was discontinued. Six days later a cough, with expectoration of foul-smelling sputum, developed, which on culture showed Pneumococcus type XIX. Sulfapyridine (2-[paraaminobenzenesulfonamido]-pyridine) was given for five days. Culture of this sputum also showed B. proteus. The patient became progressively worse. A diagnosis of abscess of the lung and empyema was made. The

abscess was drained and administration of sulfanilamide again started. Several weeks later a cerebellar fungus developed at the site of the mastoidectomy, which receded after skin grafting. The patient was discharged after six months in the hospital; the ear, which continued to discharge during her stay in the hospital, is now dry. Although B. proteus is found extensively, it is rarely pathogenic. Only 12 cases of meningitis due to this organism have been reported, and in only 2 did the patients recover. Thirteen cases of septicemia due to B. proteus have been reported, with 5 deaths.

HUNTER, Philadelphia.

Peripheral and Cranial Nerves

EVALUATION OF MÉNIÈRE SYNDROME. W. E. GROVE, Ann. Otol., Rhin. & Laryng. **50**:55 (March) 1941.

Grove suggests that in determining the cause of the Ménière syndrome more consideration be given to allergy, avitaminosis and disturbances in the endocrine balance than has been accorded heretofore. If the pathologic condition of the temporal bone described by Hallpike is present in every case, then the main pathologic feature is waterlogging or edema. This condition is probably a metabolic disturbance, but whether in water balance or in sodium ions or in both is not clear. The disturbance seems to find its greatest expression in the labyrinth, where it initiates vertigo, deafness and probably also some of the tinnitus. That all of the tinnitus does not originate in the end organ is evidenced by the fact that it persists in many cases after the labyrinth is destroyed or its nerves severed. It may be that the waterlogging is operative in the end organ and also in the central cochlear nuclei. Success with dehydration, sodium elimination and histamine treatment under proper hospital supervision suggests that the patient should be treated medically before being submitted to surgical intervention. The latter measure should be reserved for patients who have not responded to a medical regimen, who, for economic or other reasons, cannot be kept on a medical regimen or whose occupation precludes any benefit from medical treatment because of carelessness in following its routine. Of the surgical measures proposed, total section of the acoustic nerve is indicated when the hearing in the affected ear has fallen below a usable level and differential section of the vestibular portion of the nerve when usable hearing is present. These operations should not be hazardous when performed by a competent neurosurgeon.

J. A. M. A.

GLOSSOPHARYNGEAL NEURALGIA. DONALD F. COBURN and CHARLES K. SHOFSTALL, Arch. Otolaryng. **33**:663 (April) 1941.

Coburn and Shofstall report a case of glossopharyngeal neuralgia in a man aged 44 with deep pain in his left ear, the pain having begun six months previously, immediately after he drank a bottle of cold soft beverage. He had had no further pain until one month previously, but during the month had had numerous attacks. The pain seemed to start in the side of his throat, at about the junction of his throat and ear on the left side, and then shot deep into his ear. It was usually initiated by swallowing. Attacks, however, had been brought on by turning his head and occasionally occurred when he talked; blowing the nose sometimes started the pain. General physical and neurologic examinations revealed nothing significant. A trigger zone was sought in the areas supplied by the ninth nerve. A 2 per cent solution of eucupin (isoamylhydrocupreine) was injected directly through the drug membrane into the middle ear, with no relief. A 2 per cent solution of pontocaine hydrochloride was introduced into the eustachian tube, with no relief. Cocainization of the sphenopalatine ganglion had no effect. The tongue areas were anesthetized, with no effect, but when the applicator touched a point on the upper part of the pharynx directly posterior to the eustachian orifice and high up on the lateral pharyngeal wall an extremely sensitive area was found and an attack was immediately brought on. An intracranial operation was per-

formed, and the ninth, tenth and eleventh nerves on the left side were exposed proximal to their exit through the foramen of the jugular vein. The ninth nerve was crushed and divided. The patient had complete recovery, with no symptoms, but had dry taste and later complained of a bitter taste. Hearing, swallowing and other functions were not affected.

HUNTER, Philadelphia.

CHANGES IN VESTIBULAR SENSITIVITY IN MÉNIÈRE'S SYNDROME AND THEIR SIGNIFICANCE. MILES ATKINSON, Arch. Otolaryng. **33**:969 (June) 1941.

In cases of Ménière's disease the results of vestibular tests vary so greatly in different cases and at different times in the same case that they have been considered of no value. Atkinson believes this view to be wrong. His analysis shows that at times the vestibular tests give normal responses; sometimes they show hypofunction and again hyperfunction. The division of cases into those in which the mechanism is allergic (vasodilatation) and those in which it is vasospastic (constriction) is important. The histamine skin test gives a positive reaction in the allergic, or vasodilator, group. In this group the vestibular function is either diminished or unchanged, but in the vasospastic group it is almost invariably increased. In 4 of 8 cases of the vasodilator group there was hypofunction of the affected labyrinth between attacks, in 3 function was normal and in 1 the test was not done. In no case was hyperfunction found. Fourteen cases in which the reaction to the histamine skin test was negative were placed in the vasoconstrictor group. In all but 2 hyperfunction was observed on the side of the affected ear. In these 2 hypofunction was present, but the reaction to the histamine test was negative. Examination of the audiograms in the vasodilator, or allergic, group indicated bilateral conductive deafness, whereas in the vasoconstrictor group the audiogram was characteristic of perceptive deafness.

There is general agreement that the labyrinth is the site of the disturbance in Ménière's disease. Atkinson's theory that the attacks are brought about by sudden changes in the blood vessels in the vestibule, accompanied by variations either in their permeability or in their caliber, affords a simple explanation of the variation in vestibular function in different cases and in the same case at different times and for the occurrence of hypofunction in one group and of hyperfunction in the other. In the allergic group the vessels of the stria vascularis dilate, the permeability of the vessel walls is increased and more endolymph is formed. The increased pressure so induced inhibits function, making compensation impossible, and an attack of vertigo results. When the attack is over and the capillary dilatation in the stria has subsided, the pressure of the endolymph subsides. The vestibular tests may give normal reactions or may show slight hypofunction, whereas during the attacks the vestibular tests showed greater diminution of function. The more often this process is repeated the more permanent the diminution of function, with final permanent changes. In the vasoconstrictor group the modus operandi is just the reverse. Whereas the cochlea is avascular, like the lens of the eye, and depends for its nutrition on the endolymph, the maculas and the cristae rest on a rich capillary bed. Constriction of the blood supply causes imbalance and therefore vertigo. In these cases hypersensitivity of the labyrinth is found in the intervals between attacks. Atkinson accounts for this by suggesting that with permanent diminution of the blood supply to the labyrinth, either from degenerative otolith disease or from vasospasm, paresthesia with a perverted response to stimulus results, and with it a heightened response to normal stimuli, such as is seen in a limb that has "gone to sleep." This paresthesia causes the hyperfunction between attacks. Furthermore, the degree of the increased response to stimulation varies with the degree of vascular spasm, and thus there is an explanation for some of the variations in results. If the diminution of the blood supply persists over long periods a gradual degeneration may be expected to take place, and ultimately hyperfunction will give way to hypofunction. The 2 patients in this group who exhibited such hypofunction had suffered attacks over ten and twenty-one years, respectively. The change in cochlear function is also explicable

on this basis. If the blood supply to the vestibule is diminished, so is that to the cochlea, or more probably to the cochlear nerve, since the cochlea itself is an avascular structure.

HUNTER, Philadelphia.

PARALYSIS AND PARESIS OF THE VOCAL CORDS. WALTER P. WORK, Arch. Otolaryng. **34**:267 (Aug.) 1941.

Impaired movement of the vocal cords may be partial or complete and may be unilateral or bilateral. The difficulty may be due to lesions in either the central or the peripheral innervation or to ankylosis or neoplasm. The most common factors causing paralysis of the vocal cord are aortic aneurysm, tumor of the mediastinum, tumor of the esophagus and hypopharynx, goiter and lesions originating in the central nervous system. Statistics show that young females and old males are most often affected. The symptoms in order of frequency are hoarseness, tiredness, dyspnea, strangling and stridor. One-third to one-half the patients have no symptoms. When the cases following thyroidectomy are excluded, in about 33 per cent the cause of the difficulty cannot be determined.

Work reports a case of congenital bilateral fixation of the cords associated with spina bifida occulta and meningocele of the sacral region.

He summarizes his study of paralysis and paresis of the vocal cords as follows:

1. Paralysis of the recurrent nerve occurs later in life in males than in females, if paralysis associated with operation on the thyroid gland is disregarded. 2. Thirty per cent of patients with paralysis of the vocal cord have no laryngeal symptoms. Fifty per cent have no symptoms with paretic involvement of the vocal cords. 3. Transient paretic conditions of the vocal cords associated with central cerebral lesions exist; they may be unilateral or bilateral and are probably missed clinically for the most part. 4. Postoperative paralysis of the recurrent laryngeal nerves associated with thyroidectomy occurs in females and in males in a ratio of approximately 7.4 to 1. The left nerve is slightly more often involved. The median and cadaveric positions of the cords occur with equal frequency. Bilateral impairment of the vocal cords occurs about once in every 6 cases of postoperative paralysis associated with thyroidectomy, and in this group the median position of the vocal cords is most often encountered. 5. Paralysis of the laryngeal nerve may occur after one stage total pneumonectomy. 6. If one disregards cases in which postoperative paralysis is associated with thyroidectomy, the left vocal cord is more often affected by paralysis than the right. The median position of the cords is more often encountered than the cadaveric. 7. Prognosis for recovery of the vocal cords is approximately 25 per cent in cases of postoperative paralysis associated with thyroidectomy and 50 per cent in cases of paresis. Recovery, if it takes place, usually occurs within six months. 8. Prognosis for recovery from paralysis other than the postoperative type is poor (5 per cent); in the paretic group the prognosis is better.

HUNTER, Philadelphia.

Cerebrospinal Fluid

SIGNIFICANCE OF EXAMINATION OF CEREBROSPINAL FLUID FOR DIAGNOSIS OF MULTIPLE SCLEROSIS. W. KLIMKE, Deutsche med. Wchnschr. **66**:1402 (Dec. 13) 1940.

Klimke reports 211 cases of multiple sclerosis diagnosed in his clinic. In 42 cases the cerebrospinal fluid obtained from the occipital, as well as from the lumbar, puncture was normal. The author emphasizes this because he had observed in a number of cases that the occipital fluid was still normal when the lumbar fluid had disclosed pathologic changes. The fluid should be withdrawn as near as possible to the most massive focus; that is, lumbar puncture would be preferable in most cases of early multiple sclerosis. The cerebrospinal fluid showed pathologic changes in 169 (80.54 per cent) of the cases. The colloidal gold chloride test produced a left-sided curve in 137 cases and a right-sided curve in only 29 cases.

In 2 other cases the cerebrospinal fluid exhibited only mild lymphocytosis, and in 1 it showed a slight increase in albumin. Closer analysis of the fluids showing a left-sided curve disclosed no increase in protein or in cells in 32 cases, slight increase in protein (globulin) in 32 cases, a slightly elevated cell count in 21 cases and increase in proteins and cells in 51 cases. The author concludes that the colloidal gold chloride reaction, more particularly the left-sided curve, is characteristic for multiple sclerosis. More than half of the curves (59 per cent) were like those seen in cases of dementia paralytica; that is, in the first two tubes there was discoloration from blue to white. This strong discoloration was seen in nearly all cerebrospinal fluids that also had an increased protein content and cell count. However, the same deep curve was observed also in many fluids that had only an increase in the cell count or only an increased protein content and even in many fluids in which both were absent. Thus the depth of the curve cannot be dependent on an increase in protein or in cells. This manifestation was designated by Thurco as cyto-albuminocolloidal dissociation. The author thinks that in the presence of deep left-sided curves without, or with only slight, increase in cell count and protein content, the laboratory observations suggest the existence of multiple sclerosis, provided reactions for syphilis are negative. This picture is seen in no other disorder, except that in cases of successfully treated dementia paralytica there remains a deep left-sided curve; however, when the left-sided curve is not too pronounced and there is a slight increase in proteins and cells, tabes dorsalis must be thought of, if the reactions for syphilis are negative. The essential sign of dementia paralytica, that is, intense left-sided curves with moderate or severe increase in the cell count and in protein, particularly the globulins, the author observed so rarely in cases of multiple sclerosis that it can be disregarded. The 32 cerebrospinal fluids with a right-sided curve disclosed atypical pictures, associated with slight increase in cells and albumin. In 77 cases of multiple sclerosis the author was able to repeat the fluid examination several times in the course of the treatment. For 6 of the fluids the right-sided curves changed into typical left-sided curves and for 5 the curves became normal, whereas the right-sided curves in the others remained unchanged. The fluids with a left-sided curve lost the increased cell count and protein content, but the curve remained unchanged. The author concludes that the change from a right-sided to a left-sided curve, the disappearance of the increase in protein and cells and the persistence of the left-sided curve indicate clearly that the left-sided curve without increase in proteins and cells, that is, the cyto-albuminocolloidal dissociation, is the characteristic picture of the cerebrospinal fluid of multiple sclerosis and that conditions resembling multiple sclerosis and presenting a right-sided fluid curve probably are not true multiple sclerosis.

J. A. M. A.

CEREBROSPINAL FLUID IN SCIATICA. L. PRIBÉK, Klin. Wchnschr. **20**:320 (March 29) 1941.

Pribék points out that it is often difficult to differentiate sciatica from lumbago or muscular rheumatism. Differentiation of sciatica demands careful physical examination, roentgenoscopic examination of the vertebral column in different exposures, myelographic observation on the cutaneous temperature and examination of the cerebrospinal fluid. Thermoelectrical determination of the cutaneous temperature in various regions of the course of the sciatic nerve permits differentiation of lumbago and sciatica, because in sciatica the temperature of the diseased side is from 0.3 to 0.5 degree C. (0.54 to 0.9 degree F.) lower than that of the healthy side while in lumbago the temperature is the same on the two sides. The author performed spinal puncture and examination of the fluid in 20 cases. The pressure of the fluid varied in different disorders. In muscular rheumatism it was between 12 and 15 cm. of water; in lumbago it averaged 15 cm.,

and in sciatica, 21 cm. The number of cells was increased in sciatica, even if the fluid was clear. The total protein and the sugar contents were usually increased in sciatica. The cerebrospinal fluid of patients with lumbago or muscular rheumatism was usually normal.

J. A. M. A.

CEREBROSPINAL FLUID IN MULTIPLE SCLEROSIS. O. SEUBERLING, Nervenarzt **13**:359 (Aug. 15) 1940.

Seuberling reports the serologic picture of the cerebrospinal fluid of 140 patients with multiple sclerosis observed at the neurologic clinic of the University of Würzburg. The results obtained, together with those of three other German clinics, suggest that the cerebrospinal fluid of 75 per cent of patients with definitely established multiple sclerosis shows pathologic changes. The author was able to corroborate the observation of several other investigators that a correlation exists between changes in the cerebrospinal fluid and severity of the multiple sclerosis. Pathologic alterations of the cerebrospinal fluid occurred twice as frequently in patients with severe multiple sclerosis as in those with mild disease. During the acute attack only 2 per cent of the patients had normal fluid. The largest percentage of normal fluids was obtained from patients whose disease had lasted less than a year. In the course of the first attack 98 per cent of the patients show pathologic changes in the cerebrospinal fluid, but in more than one half of these the fluid becomes normal later. In patients with chronic multiple sclerosis the fluid is much less likely to become normal after an exacerbation. Efforts have been made at the author's clinic to establish a specific reaction for multiple sclerosis by paying particular attention to the lipoid metabolism and the lipolytic ferments in the cerebrospinal fluid. No characteristic sign or behavior has thus far been detected. At this clinic spinal punctures have not been found harmful except for occasional retention of urine for about a day. Punctures should not be made in cases of multiple sclerosis in which foci are suspected to exist on the floor of the fourth ventricle and in which bulbar and vagal symptoms appear. The author observed coma of several days' duration following a puncture in a case of this type.

J. A. M. A.

Muscular System

MYASTHENIA GRAVIS. S. T. LEVETHAN, A. J. FRIED and M. J. MADONICK, Am. J. Dis. Child. **61**:770 (April) 1941.

In a review of the literature concerned with cases of myasthenia gravis in children under 17 years of age, the authors found only 34 instances, the average age of the patients being 11.8 years; only 8 patients were under the age of 10 years. They report 1 case of their own, that of a 9 year old girl who had previously been treated with prostigmine bromide, with an immediate beneficial result. She was admitted to the hospital in collapse, was given prostigmine methylsulfate intravenously and within fifteen or twenty minutes was breathing calmly and appeared improved. She was placed under a regimen of 45 mg. of prostigmine bromide given orally four times daily for some weeks, during which her condition continued to be good. On the advice of another physician, this medication was discontinued after her discharge from the hospital. She was readmitted shortly afterward, with a marked increase in the severity of her symptoms and in a few days she died. The final diagnosis was myasthenia gravis and bronchopneumonia. Autopsy was not performed. The authors suggest that oral administration of prostigmine bromide, supplemented with ephedrine sulfate, potassium chloride and occasionally guanidine, is the most efficient form of treatment now available.

WAGGONER, Ann Arbor, Mich.

THE HEREDITY OF PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY. WALTER S. POLACHECK, Am. J. Dis. Child. **61**:1251 (June) 1941.

Polacheck presents the family tree in a case of pseudohypertrophic muscular dystrophy, in which 10 male members in three generations had the disease. From this study and from a review of the literature, he states, "The disorder is clearly seen to be a sex-linked mendelian recessive trait." The onset of the disorder was between the fourth and the seventh year of life and progressed slowly to fatal termination sometime between the ages of 10 and 17 years.

WAGGONER, Ann Arbor, Mich.

INVOLVEMENT OF THE THYMUS IN MYASTHENIA GRAVIS PSEUDOPARALYTICA. C. BOMSKOV and G. MILZNER, Deutsche Ztschr. f. Chir. **254**:99 (Oct. 19) 1940.

Bomskov and Milzner investigated Adler's theory of involvement of the thymus in myasthenia by experimenting on some 120 rats and 30 guinea pigs both with the specific thymus hormone as well as with extracts prepared according to Adler's method. They arrived at the conclusion that if the endocrine system is involved it is not the thymus but the adrenal cortex impairment of which is primarily responsible for all myasthenic phenomena. Myasthenia is defined as abnormal muscular fatigue, demonstrable in spontaneous movements and on electrical stimulation. Anatomically nonspecific, so-called lymphocytic, infiltrations are most frequently observed in the muscles. According to Adler, the implantation of dog or calf thymus glands in dogs, the administration of certain thymus extracts and the injection of blood of myasthenic persons provoke grave myasthenia with complete prostration in some dogs. Adler also holds the view that myasthenia associated with exophthalmic goiter and adynamia observed in Addison's disease are true myasthenia, since Jolly's reaction is positive and prostigmine bromide effects prompt amelioration.

In their experiments the authors employed the specific thymus hormone and the extracts prepared according to Adler's formula in very high concentrations. Rats and guinea pigs were used instead of dogs because adrenalectomy regularly induces typical adynamia in these animals and thus makes them excellent material for cortical hormone experiments. In no case were the authors able by either method to induce myasthenic reactions. The authors believe that the discrepancy between Adler's and their results is due in part to the inadequacy of Adler's procedure. Several of his dogs died of pneumonia shortly after the test; abscesses were also observed after implantation. However, for them the crux of the experiments lies in the fact that Adler was unable, in spite of prolonged injections of thymus extract, to induce the clinical phenomenon of fatigue, specific for myasthenia. Adler, they think, also overestimated the diagnostic value of Jolly's reaction, for he found myasthenia in numerous cases of exophthalmic goiter, the frequency far exceeding that of all other investigators. The authors believe that there is no primary connection between myasthenia and the thymus gland. J. A. M. A.

PROSTIGMINE TREATMENT OF MYASTHENIA GRAVIS, WITH COMMENT ON THE THEORY OF THE ACTION OF PHYSOSTIGMINE AND PROSTIGMINE. MARIE LÜSCHER, Schweiz. Arch. f. Neurol. u. Psychiat. **45**:397, 1940.

In a review of various contributions to the pathogenesis of myasthenia gravis, Lüscher expresses the opinion that the disease is due to a disturbance of the function of acetylcholine in the transference of impulses from nerve to muscle. Prostigmine and physostigmine are believed to inhibit the action of an acetylcholine-splitting esterase. Salmon's investigations indicate that myasthenia gravis is accompanied by hypotonia of the parasympathetic and by hypertonia of the sympathetic nervous system. The "vagus substance," which is liberated on stimulation of parasympathetic nerves, is thought to be identical with acetylcholine. Since acetylcholine is also concerned in the transmission of impulses over the myoneural junctions of skeletal muscles, the view is expressed that myasthenia gravis is characterized by hypotonia of the entire cholinergic system.

Lüscher reports a case of myasthenia gravis in which a recent exacerbation of symptoms had caused the patient to seek treatment. The case is somewhat unusual in that at the time of onset, seventeen years previously, ptosis and diplopia were preceded by weakness of the hands. Physostigmine salicylate was given orally in doses of 1 mg. three times daily, with little effect. A subcutaneous injection of 1 mg. of prostigmine methylsulfate was followed immediately by double vision, apparently the result of spasm of the extraocular muscles, and, within a few minutes, by tonic spasm of the muscles of mastication, congestion of the head and marked sweating. The patient next experienced clonic spasms of the muscles of the lower extremities and upper part of the abdomen, as well as of the levator palpebrarum muscles. The immediate effects of the drug subsided within forty-five minutes, and the patient was free of his myasthenic symptoms for several hours. Injections of 0.5 mg. of prostigmine methylsulfate were well tolerated, but the benefit obtained was transient. Further injections of the drug in doses of 1 mg. were without undesirable effects, and the patient was given an injection of this amount every day. The oral administration of physostigmine salicylate was later replaced by that of ephedrine in doses of 10 to 20 mg. three times daily, and a prolonged rest cure was ordered. Under this regimen the myasthenic symptoms became much less severe.

Prostigmine has proved to be the best medicament for the treatment of myasthenia gravis. The experience of some authors indicate that its effect may be either enhanced or prolonged by the administration of potassium salts. Prostigmine seldom has undesirable effects in cases of myasthenia gravis, apparently because of hypotonia of the cholinergic system. There is evidence to suggest that the benefit obtained from the use of prostigmine may be due, in part, to its "amphotropic action" on the sympathetic nervous system. DANIELS, Denver.

CHANGES IN THE THYMUS ASSOCIATED WITH MYASTHENIA GRAVIS. K. BOMAN, Nord. med. (Hygiea) **10**:1625 (May 24) 1941.

Boman states that hyperplasia of the thymus or thymomas have been established in at least 50 per cent of the cases of myasthenia gravis. Guanidine-prostigmine treatment of myasthenia gravis is considered the best medical therapy. Roentgen irradiation of the thymus has been ineffective. To date it is not possible to evaluate the treatment of myasthenia gravis by the removal of areas of hyperplasia in the thymus or of thymomas because of the high mortality due to the technical difficulties in operation and the lowered resistance to infections in the postoperative course. Although the genesis of myasthenia gravis is still uncertain, a causal relation between the symptoms of the disease and the changes in the thymus is indicated. When the patient has survived the operative treatment a striking improvement has resulted. In the most successful cases the myasthenia has gradually assumed a latent form and given symptoms only in connection with exertion or infections. The changes in the thymus and the thymomas seen in cases of myasthenia gravis vary greatly, both clinically and histologically. The morphologic differences may perhaps be the expression of different functional conditions, which might explain the variation in the clinical course of myasthenia gravis. In the 2 cases described there was rapid tiring on exertion without the involvement of any special group of muscles. J. A. M. A.

Congenital Anomalies

CONGENITAL ABSENCE OF THE CRANIAL VENOUS SINUSES ON THE RIGHT. HENRY L. WILLIAMS and O. E. HALLBERG, Arch. Otolaryng. **33**:78 (Jan.) 1941.

In a previous case Williams reported on congenital absence of the descending portion of the sigmoid sinus, with the lateral sinus reduced to the size of a thread. A large vein following the course of the superior petrosal sinus left the skull by way of the foramen for the emissary vein of the mastoid process. This case, reported in 1930, was the first in the literature in which the congenital absence

was found at operation. In 1936 Hoople reported a case of congenital absence of the sigmoid sinus. In 1937 Furstenberg reported 7 cases of anomalies of the sigmoid sinus encountered at operation and an eighth case in which he observed the condition in the dissecting room. In none of the cases was the sigmoid sinus absent. Laff, in 1930, thoroughly reviewed the condition from a developmental standpoint. A second case found at operation by Williams is reported. In a child of 11 months an operation on the right mastoid was performed and a huge epidural abscess found. The bone covering it was widely removed until healthy bone was obtained. With this wide exposure of the brain, the sigmoid or lateral sinus could not be found, or any evidence of the superior or inferior petrosal sinus. The recovery was uneventful. The child was discharged on the eleventh day after operation.

The author believes that the infection of the blood stream with Streptococcus haemolyticus may have been caused by extension of the disease to the lateral sinus of the opposite side, although he found no definite evidence of such infection at operation. The small venules of the dura or the veins of the diploe of the skull may also have been involved, although no evidence of encephalitis or osteomyelitis was observed. Finally, the presence of a jugular bulb was not absolutely eliminated, and entrance to the blood stream may have been through the floor of the middle ear, although the inferior surface of the pyramid was exposed in a vain attempt to find such a structure.

HUNTER, Philadelphia.

ARNOLD-CHIARI MALFORMATION: DIAGNOSIS, DEMONSTRATION BY INTRASPINAL LIPIODOL AND SUCCESSFUL SURGICAL TREATMENT. R. D. ADAMS, R. SHATZKI and W. B. SCOVILLE, New England J. Med. **225**:125 (July 24) 1941.

Adams and his co-workers report 2 cases of the Arnold-Chiari malformation; in 1 there was no meningomyelocele. Clinically the patients had similar symptoms, falling into five types: increased intracranial pressure, involvement of cranial nerve, compression of the brain stem, compression of the spinal cord and cerebellar signs. The following symptoms were manifested in each case: (1) occipital headaches, vomiting, nausea and papilledema; (2) disturbances pointing to bilateral lesions of the seventh, ninth, third, tenth and twelth cranial nerves; (3) disturbances of conjugate movements of the eyes and vertical nystagmus; (4) bilateral signs of involvement of the pyramidal tract, and (5) disturbance in gait, tremor and incoordination of movement. Some degree of platybasia is often found in the Arnold-Chiari syndrome; in all probability it is an associated congenital anomaly of the skull. Lumbar puncture and myelographic examination were of diagnostic aid. Lumbar puncture showed a complete block in the dynamics of cerebrospinal fluid. The protein content of the spinal fluid was increased. The intraspinal injection of iodized oil gives an almost diagnostic picture; it outlines the bifid projection of the two herniated cerebellar hemispheres. Most operations on patients with this malformation have been unsuccessful. The patient often fails to regain consciousness or dies suddenly during convalescence, presumably from compression of the medulla. Probably the cervical portion of the spinal cord and the cerebellum should be decompressed, and no attempt should be made to liberate the nerve structures in the posterior fossa from the arachnoid adhesions. Any manipulation that causes a sudden change in the spatial relations of these structures may lead to death. Both of the authors' patients survived the operation, even though more than a simple decompression was done, and continued to improve for the eighteen and six months that they were followed. Preoperative ventricular drainage was not attempted.

J. A. M. A.

SPASMODIC QUADRIPLEGIA, WITH FAMILIAL IDIOCY AND DEAF MUTISM. C. JAKOB and A. SCARAVELLI, Rev. neurol. de Buenos Aires **5**:283 (Oct.-Dec.) 1940.

Jakob and Scaravelli report the occurrence of these abnormalities in a family of 8 brothers and sisters. The parents are farmers of normal intellect and education for their social sphere. They are nonconsanguineous, nonsyphilitic and non-

alcoholic. Some of the father's brothers had mental abnormalities. They died unmarried. The normal brothers and sisters of the father had normal children. The family of the mother is normal. The couple had 10 children, all of whom had a normal delivery. One of the children was apparently normal up to the age of 15 years, when she had an epileptic attack, fell from a horse and died. Another was apparently normal up to the age of 10 months, when he stopped growing and lived for twenty-three years in his cradle, an idiot. Another was an idiot with epilepsy from early childhood and died at the age of 16 years. Seven, between the ages of 30 and 45, are living. None of the children had meningitis in infancy or childhood. All have spasmodic quadriplegia, deaf mutism, idiocy and epilepsy. Some crawl on their knees, and some exhibit strabismus. The authors made an anatomic study of brains of human embryos and anatomopathologic studies of brains of cadavers of idiots with congenital spasmodic quadriplegia, epilepsy and mutism. The brains of idiots exhibited symmetric tuberous dysplasia or hypoplasia of the rolandic areas, symmetric hypoplasia of the rolandic, temporal and parietal areas and of the pyramids and corpus callosum and, in some cases, microgyria and pachygyria. The authors believe that these abnormalities are due to symmetric lack of development of the rolandic, parietal and temporal areas during the second and third months of embryonic development, with consequent establishment of a condition of the nervous tissues which simulates corticosubcortical tuberous sclerosis, early hypoplasia of the pyramids and corpus callosum and secondary hypoplasia of the parietal and frontal lobes. Heredity is a factor in the absence of other pathogenic factors. The existence of parallel recessive neurogenic defects in both parents is a plausible explanation of the abnormalities in the family reported by the author.

J. A. M. A.

Diseases of Skull and Vertebrae

NEUROLOGIC SYMPTOMS AND CLINICAL FINDINGS IN PATIENTS WITH CERVICAL DEGENERATIVE ARTHRITIS. S. R. METTIER and C. S. CAPP, Ann. Int. Med. **14**:1315 (Feb.) 1941.

Mettier and Capp analyzed the symptoms suggestive of cervical nerve root origin in 30 patients presumably having osteoarthritis. Attempt was made to correlate the symptoms with the changes seen in the cervical vertebrae in roentgenograms taken in anteroposterior, lateral and oblique projections. The patients examined had symptoms characteristic of cervical radiculitis. Most of them were between 40 and 60 years of age. Only 3 were less than 40 years of age. The symptoms complained of were pain, rigidity of the neck and muscular weakness of the hand or arm. The onset of pain was usually abrupt and was localized in and about the shoulder, especially about the insertion of the deltoid muscle, or radiated down the arm into the fingers. As a rule these symptoms appeared months, or even years, before there were any complaints of discomfort in the neck. Usually the pain was unilateral. Some patients complained only of numbness and tingling in the fingers or of a drawing or dead, aching sensation in the muscles of the arms. Restriction of use of one upper extremity was a common complaint. There was no atrophy of the muscles of the hands, arms or shoulder girdle. The arm reflexes were normal. The presence or absence of arthritis in the cervical vertebrae was determined by roentgen observations. Marked hypertrophic changes were observed in 18 patients. These consisted of circumferential osteophyte formation which projected into the intervertebral canal from the superior or inferior vertebral margin, causing slight to marked narrowing of the foramen, depending on the size of the hypertrophic spur. The osteoarthroses were more frequently on the left side. In the areas of exostosis the intervertebral disk was thinned out, causing slight narrowing to almost complete obliteration of the intervertebral space. The sites of predilection were between the fifth and sixth and the sixth and seventh vertebrae. The symptoms of 7 other patients were similar, but the roentgen signs of osteoarthroses were minimal in degree. There was a minimal to slight degree

of osteophyte formation on the adjacent surfaces of the vertebrae, usually the fifth and sixth. This was accompanied by narrowing of the intervertebral disks in only 3 patients. In most of the patients there was some sclerosis of the articular facets. In the remaining patients there was no apparent abnormality of the articular facets or evidence of proliferative new bone formation at the vertebral margins, noticeable narrowing of the intervertebral foramens or thinning of the intervertebral disks. From the roentgen study it is evident that the combination of narrowing of the intervertebral foramen by the ingrowth of the marginal osteophytes and the decrease in the vertical diameter of the foramen, as seen in the 18 patients, may result in impingement on the nerve trunk as it passes through the involved foramen or may affect the sympathetic fibers controlling blood flow. The reason that this process picks out the sensory fibers and does not also involve the motor fibers may be the fact that the motor fibers are fewer and comprise a bundle only one-third the size of the posterior sensory fibers. Therefore actual diminution in the size of the nerve trunk may be sufficient to give rise to the radicular syndrome. It is unlikely that a similar process can adequately explain the neurologic symptoms arising in the other patients, as there was no radiopaque material in the intervertebral foramens suggesting impingement on a nerve bundle. The syndrome is of relatively frequent occurrence and, as a rule, is inadequately treated. The 30 patients were encountered in less than three months. Many had resorted to forms of treatment not regularly recognized by the medical profession. Those whose treatment was basically manipulative had definite relief. In the authors' clinic treatment consisted of application of heat to the neck, massage, manual traction and manipulation. Most of the patients were relieved of pain.

J. A. M. A.

BECHTEREW'S SPONDYLARTHRITIS ANKYLOPOIETICA, WITH REFERENCE TO INCIPIENT STAGES AND ATYPICAL FORMS. M. ELTZE, Med. Klin. **36**:1125 (Oct. 11) 1940.

Eltze reviews the pathologic anatomy and then describes the clinical picture of completely developed ankylopoietic spondylarthritis. Since early recognition is of great importance for effective treatment, he gives special attention to the incipient stages. The disease is sometimes preceded by rheumatic purpura or by nodose rheumatism of the scalp. Iritis may be the clinical sign of rheumatism. Neuralgia in the sciatic nerve, particularly if it is bilateral, and prolonged pain in the back make it advisable to resort to roentgenoscopy of the pelvis. This will frequently disclose changes in the sacroiliac articulation. The articular clefts are indefinite, and the articular surfaces appear as if gnawed on. Inflammatory niches are interspersed with narrow bone bridges, which gradually become wider. Cloudy densification of the bone appear near the articular clefts. From one to three, or even more, years may elapse before these changes become visible in the roentgenogram. Limitation of the respiratory excursion likewise may occur early. The sedimentation speed of the erythrocytes is nearly always increased during the early stages. The rigidity of the vertebral column should make the observer think of ankylopoietic spondylarthritis. In the severe forms complete stiffening and ossification take place within a few years or a decade and the patients become completely helpless. The benign form develops more slowly, in that two decades may elapse before the patient becomes incapacitated; the stiffening is usually not so severe in these cases. The atypical forms of ankylopoietic spondylarthritis are characterized by the fact that not only the large joints near the trunk (shoulder and hip joints) are diseased but also the more distal ones, that is, the elbow hand, finger, knee and foot joints. Rheumatic heart disease may also exist. The recognition of the atypical forms is difficult because the clinical symptoms are often slight in spite of chronicity. However, if Bechterew's spondylarthritis ankylopoietica is thought of and sought, diagnosis is possible, particularly if the vertebral column is held rigid and the sacroiliac joint exhibits changes. To differentiate ankylpoietic spondylarthritis from spondylosis, it should be considered that

spondylosis is due to wear and develops in persons of advanced age whereas ankylopoietic spondylarthritis develops in the second or third decade of life, although it may remain long unrecognized, so that it is not diagnosed until spondylosis causes the first complaints. Spondylarthritis ankylopoietica involves the entire or large portions of the vertebral column, whereas spondylosis is limited to a few vertebrae. There is no flattening of the physiologic lumbar lordosis, no increase in the sedimentation speed of the erythrocytes and no change in the sacroiliac joint in patients with spondylosis. The bridge formations on the vertebrae are thick in spondylosis, thin and shell-like in ankylopoietic spondylarthritis. The vertebral bodies are of glasslike transparency in ankylopoietic spondylarthritis, whereas their density is rather increased in spondylosis. J. A. M. A.

OSTEOMYELITIS OF THE FRONTAL BONE. T.MASUOKA, Bull. Nav. M. A., Japan **29**:879 (Dec.) 1940.

The incidence of osteomyelitis of cranial bones is rare, the statistical survey of 909 cases of osteomyelitis treated in the Tsukiji Charity Hospital, Tokyo, revealing only 0.22 per cent in the fifteen year period. The first patient seen by Masuoka was a girl 18 years old who had a staphylococcic infection of the frontal bone following an injury to the forehead three years previous to admission to the hospital. With local anesthesia the infected material was removed, together with two sequestrums embedded in granulomatous tissue; the patient went on to uneventful recovery. The second patient was a girl 4 years old in whom frontal osteomyelitis followed abscess formations over the upper eyelids on both sides. The suppurative process extended into the intracranial tissues, causing an abscess of the frontal lobe of the brain and leptomeningitis of the base of the brain. The patient died. The author strongly recommends early and radical removal of the infected tissues, together with such chemotherapeutic measures as administration of sulfanilamide in full doses. J. A. M. A.

Society Transactions

MICHIGAN SOCIETY OF NEUROLOGY AND PSYCHIATRY

RAYMOND W. WAGGONER, M.D., *President, in the Chair*

Regular Meeting, Sept. 11, 1941

Tardiness of Rational Psychotherapy. DR. CLARA HAPPELL, Detroit.

The development of psychology, no less than the history of medicine in general, bears witness to the reluctance of mankind to give up a belief in magic for the observation of facts. It is claimed that infantile delusions of grandeur, existing side by side with the desire for infantile dependence, are responsible for this. Both persist in spite of partial "growing up" of the human individual and humankind. These conceptions were established through the study of the neuroses of the present time.

Rational psychotherapy, while making use of the desire for dependence, aims at the transformation of the neurotic into the adult personality. It attempts to substitute adequate methods, which are at the disposal of the adult mind, for the antiquated, infantile mechanisms used heretofore.

DISCUSSION

DR. JOHN M. DORSEY, Detroit: I thank Dr. Happell for her excellent presentation of gentle, effective hints for furthering understanding of rational psychotherapy. The observation that anxiety may be a means of blocking that understanding is a valuable one. Fear, as the recurring terms "reassurance" and "encouragement" in many psychotherapeutic efforts attest, is well known as the traumatic emotion. Fear, as the motor of repression, brings about disintegration of the personality and scattered individuality. Not just the supply of helpful ideas but the nature of their mobilization determines personality integration. For example, three centuries ago Sir Francis Bacon observed, "First of all, errors of the past must be destroyed, the illusions and prejudices of our reason. And in such a way our reason will be pure and vacant like an infant's. After that, our next step must be the choice of experiences and of facts by experiment and observation." Fear, particularly in the form of fear of fear, can explain why such wisdom is too seldom found to be effectively mobile in present day education.

Psychiatric Treatment. DR. LEO H. BARTEMEIER, Detroit.

This paper is concerned with increasing the effectiveness of nonanalytic psychotherapy. The first three interviews with a patient are described in detail for the purpose of demonstrating those factors which are too frequently overlooked. Among these, the seemingly insignificant remarks of the patient and his attitude toward the psychiatrist are indispensable to the therapy.

DISCUSSION

DR. RICHARD STERBA, Detroit: In his demonstration of a particularly difficult case, Dr. Bartemeier emphasized the importance of the psychiatrist's attitude toward a new patient in the first interview. He pictured the patient's "preformed transference," shaped by similar former experiences, infantile and adult, and pointed out that this picture, if not too greatly disturbed by personal influence, can show the psychiatrist the characteristic elements which play an important role in the patient's mental disturbance. An atmosphere of freedom and relaxation

enables the patient to reduce his tension and defenses; a receptive attitude on the part of the psychiatrist is one of the main factors by which this is achieved, but there is also another. Intangible signs of sympathy, empathy and interest make the patient feel that he has turned to some one who will understand and accept him, even in matters against which he himself has set up strong defenses. The personality of the physician therefore plays an extremely important part in psychotherapy.

DR. J. CLARK MOLONEY, Detroit: I wish to emphasize that which Dr. Bartemeier has already emphasized, namely, the attitude of acceptance toward the patient. It has been my policy, when a new patient comes to me, to keep in mind a realization that he may feel that he is not acceptable to me. I attempt to allay the patient's fears and to give him a feeling of acceptance. Nothing can be done in an analysis until the patient has a complete feeling of confidence in the sincerity of the analyst. It is only after the patient has obtained some degree of security in the analytic situation that the analysis really begins.

DR. IRA M. ALTSHULER, Detroit: Dr. Bartemeier has frankly admitted that the success of his therapy was not so much the technic as the factor of rapport. Dr. Sterba, in his discussion, too, expressed the belief that the rapport is the crux of the matter. It matters not whether the therapeutist is of the freudian school, an Adlerian, a Steckelian, a follower of Jung or a psychobiologist, the rapport is the thing which determines the success or failure of the therapy.

ILLINOIS PSYCHIATRIC SOCIETY

WALTER H. BAER, M.D., *President, in the Chair*

Regular Meeting, Oct. 2, 1941

Psychiatric Inventory of One Hundred Cases of Indecent Exposure. DR. A. J. ARIEFF and DR. D. B. ROTMAN, Chicago.

Indecent exposure is the most common, constituting 35 per cent, of all sex offenses for which commitment is made to the Municipal Psychiatric Institute. The age peak of offenders is in the third decade, when the incidence is 35 per cent. Eighty-four per cent of such offenses occurred before the age of 40. All offenders were males. Only 4 per cent were Negroes. In most cases the offense occurred near or in the home; in the others, in public places. Seventy-four per cent of offenders exposed themselves in broad daylight. Sixty-eight cases were analyzed as to the religion and church attendance. Thirty-six of the offenders were Catholic, 34 Protestant, 5 Jewish and 3 Christian scientists. Of these, 32 attended church regularly. Twenty-nine had completed less than eight grades of school, and 2 were illiterate; 25 had reached the eighth grade; 21 had had two years of high school; 13 had had four years of high school and 12 had had college work. Of the 100 patients, 62 were single and 38 married. Marital maladjustment was in evidence in the latter group, even though 23 had children. Sixty-six had a history of previous antisocial incidents other than exhibitionism which had resulted in arrest. Of the institutional patients, 6 had schizophrenia, 13 were mentally defective, 1 was in an alcoholic paranoid state, 1 had dementia paralytica and 1 senile dementia. Of the noninstitutionalized patients, 13 were in a constitutional psychopathic state, 26 had a compulsive neurosis, 16 borderline mental deficiency, 15 dull normal intelligence and 4 a borderline schizoid state. Alcoholism was a contributing factor in 28 cases.

Thirty-eight patients admitted guilt and 24 denied it. Six persons said they were dazed at the time of the offense. A rational explanation was not forthcoming. Eleven admitted sexual pleasure. Fifteen said they had marital dis-

satisfaction. Lack of home harmony was present in 12 cases. In 10 instances the patient was an only child. Twenty-one patients had had no previous heterosexual experience. Eight patients admitted practicing perversions. Thirty-one patients stated that they masturbated, even when a heterosexual adjustment had supposedly been made. A phylogenetic explanation appears to be the most plausible at present.

DISCUSSION

Dr. A. C. Ivy, Chicago: Several years ago, as some may recall, Drs. Greene, Burrill and I discovered how to modify in the rat the development of all sex organs, with the exception of the gonads, by administering estrogens to the pregnant mother. When an exhibit on this subject was presented at the annual session of the American Medical Association in San Francisco, many physicians who visited the booth were more interested in homosexuality than they were in anomalies in the development of sex organs and asked us about the sexual behavior of these intersexed animals. As a result, I became interested in the question of homosexuality. My co-workers and I have seen a number of patients with different types of intersexuality or maldevelopment of the sex organs, and from none of these persons have we been able to obtain any history of homosexuality. I was particularly interested in the subject of homosexuality and disorders of sexual behavior from the standpoint of "sex hormones." I posed the question: "Is the disturbance of the production of 'sex hormones' in any way related to the problem of homosexuality and other abnormalities of sexual behavior?" I attempted to make a complete analysis of the question from a biologic and physiologic standpoint and to gather from the literature all the evidence bearing on the various portions of the analysis. I showed my analysis and the results of the survey of the literature to Dr. Arieff—and that is why I am here tonight. I am not convinced by any evidence available in the literature that an abnormality in the production of the "sex hormones" is in any way concerned with the production of the phenomena of homosexuality or any other so-called abnormal sexual behavior. So far as the rat is concerned, it seems to me clearly established that the "sex hormones" are not specific for sexual behavior. If one castrates a male rat, three to six weeks later all significant male sexual behavior will disappear. Of course, the normal and the castrated male rat manifest some homosexual activity, but the castrated male rat does not copulate or ejaculate. However, if the castrated male rat, which is not showing significant male sexual behavior or which does not copulate or ejaculate, is treated with estrogen in rather large doses, significant male sexual behavior, including copulation and ejaculation, will occur. This shows that the "sex hormones" are nonspecific in the adult rat as regards their excitation of the significant features of male sexual behavior. Both androgen and estrogen cause hyperemia and other changes in the genitalia which are necessary for the excitation and conditioning of the sex urge in lower animals. It is true that the destruction of a region in the posterior portion of the hypothalamus in the adult animal will abolish sexual behavior. Such a lesion probably destroys one of the significant centers concerned in the manifestation of the sexual reflex pattern. It is easy to postulate that androgen, for example, during prepubertal development organizes the center so that the significant features of the male behavior pattern result. This has not been proved because genetic and environmental factors have not been ruled out.

As I am not familiar with the subject of sexual exhibitionism, I cannot visualize how an abnormality in the production of "sex hormones" might be concerned. In a number of articles it has been claimed that the production of "sex hormones" is abnormal in cases of homosexuality. However, in no instance have the assays been made in an adequate manner. Too frequently the urine has been collected and sent to a commercial laboratory for assay. Even in the hands of experts assaying the same product, the value of estrogenic activity varies 25 per cent, and sometimes as much as 50 per cent. In our opinion, no assay is complete until it has been made on 20 rats whose response to a known dose of crystalline estrogen has been determined beforehand and the significance of the differences has been analyzed statistically.

I shall be interested in the personality studies that Dr. Arieff and Dr. Rotman propose to make on their patients. I expect that the results of personality and environmental studies will be of greater interest with regard to the cause of exhibitionism and homosexuality than the results of "sex hormone" assays.

DR. EUGENE I. FALSTEIN, Chicago: The experience which my associates and I have had with cases of so-called indecent exposure is confined in the main to young adolescent offenders. Since most cases of this type are seen at the Juvenile Court and the offenders are usually referred to the Institute for Juvenile Research for examination, it is not surprising that the lowermost age level mentioned by Dr. Arieff and Dr. Rotman is that at which the authority of the juvenile court ceases and is taken over by the municipal or the criminal court.

This form of perversion, representing as it does a frank, uninhibited and direct expression of sexual behavior, is ordinarily suppressed and sublimated, with the development of reaction formations of one type or other, or it may be expressed in the more common psychoneurotic symptoms, the negative of perversions, as a disguised form of gratification. Conversion hysteria offers the best example of this solution. If manifest after infancy and childhood, exhibitionism of the variety alluded to in this paper is always evidence of a psychopathologic state in our cultural setup. Cultural changes play an important role, for today women are permitted tacitly to exhibit their charms in an almost unrestricted fashion. In a brief discussion of this sort it would be impossible to go into detail regarding studies of feminine psychology, the problem of castration, etc. It is generally recognized that the woman can adopt with greater ease what for her is the more socially acceptable, passive role. The relatively low incidence of a parallel exhibitionistic problem in women may be explained by a variety of factors. One should not assume, however, that exhibitionism is unheard of in women. For one thing, it would be more difficult to conceive of a hue and cry, with calls for the police, in the case of the woman who invites sexual attention from a man through exhibiting herself than would be the case if the tables were reversed. One would expect such a strong force as exhibitionism (or scoptophilia) to break through the defenses at certain important life periods in which psychobiologic changes are most pressing and outstanding. Adolescence and the climacteric are the best examples. Anything, too, that weakens the repressive forces, such as organic disease of the brain or a psychosis, or anything that affects the person's judgment, such as mental deficiency, will often permit of open exhibitionistic trends. The latter are often the earliest signs of the changes of dementia paralytica, senility, etc.

My experience with adolescent offenders and one or two older persons, most of whom have been studied and treated over varying periods, has usually revealed the presence of distorted conceptions of sexuality that date back to the first impressions of childhood. Usually sexual relations are conceived of as exceedingly sadomasochistic experiences, with the man in the role of an aggressor and attacker. In most of the cases a strong, forbidding and dominating parent, usually the father, has continued to perpetuate in the child the feelings of weakness and impotency that are so commonly a part of the child's self regard sexually. There is a great deal of concern with the penis, and in most of the cases that I have encountered there have been effeminate personality characteristics, considerable passivity, with passive homosexual trends, and a great deal of masturbation.

In the case of a 26 year old man who was a recidivist at the Municipal Court, the exhibitionism occurred in broad daylight, usually near his home, at times when he was no longer able to tolerate feelings of inadequacy and femininity that were enhanced from day to day by a domineering father, who attempted to control his son's every activity. The son, in exposing his genitals and masturbating before a woman, appeared to be trying to show her that he was a man, inviting her to look and to be convinced. To have gone further would have involved aggressiveness of which he felt incapable and fearful. Treatment of both son and father resulted in feelings of greater independence in the boy, who was given to feel he could go out with girls, work and be more self sufficient. While he visited a

prostitute regularly at the outset, his heterosexual contacts gradually embraced all kinds of girls. He obtained a regular position and felt much more adequate and secure.

A boy of 14 who lived alone with his mother and father, the former being rather seductive and overprotective and the latter extremely moralistic and strict, was finally apprehended after having indulged for a year in a "lone wolf" type of stealing and burglarizing, associated with peculiar erotic reactions as he was doing what was forbidden and similar sensations as he awaited apprehension and punishment. When he was finally caught and the outlet provided by his stealing closed to him through various circumstances, he began to masturbate and shortly was found in a field exposing himself to a middle-aged woman. His defensiveness made him a difficult boy to treat, but repeated interviews over a period of six months altered his basic conceptions of sexuality and have not been followed by any recurrence of the exhibitionistic behavior.

Another 14 year old boy exposed himself in a woman's toilet to which he obtained admission, and carried out his conception of what was expected of him by striking a girl with a club.

Many of the boys referred to us through the Juvenile Court have been guilty of exposure and masturbation in darkened theaters, where they seat themselves beside eligible-looking girls and women. One such boy of 17 was repeatedly successful in obtaining approving collaboration from women before he was finally arrested. Apprehension and the court experiences are often sufficient to prevent further recurrences of this type of behavior.

When sexual intercourse as such is viewed as a hostile, destructive or abhorrent experience, or when in the process of psychosexual development important traumatic factors result in an early infantile or childhood fixation on some of the many and diverse expressions of the sexuality of that period, it will usually be found difficult to attain that which is expected of the sexually mature person. This inability will enhance the feelings of inferiority, weakness and impotency which have been produced psychologically and will often result in the weak, abortive attempt at sexual expression that is personified by the exhibitionism. Anything that results in organic loss of potency will undoubtedly result in a similar, more or less panicky, attempt to restore the narcissistic need for self respect as a sexual person.

In a case analyzed by Dr. Adelaide Johnson, the exhibitionism appeared when the man felt frustrated by a domineering mother, and the activity was associated with feelings of rage and defiance, which he acted out on the outside against other women. This case illustrates the importance of the hostile, aggressive, shocking component in this type of activity.

Group 2, in the authors' classification, is obviously the more important from the psychologic standpoint. I should like to know more about the criteria for the subgrouping. The single outstanding characteristic of most of the cases in the group consists in a prominent psychosexual pathologic state, which would warrant intensive study of each individual case to supplement this interesting statistical study.

DR. A. J. ARIEFF, Chicago: There is a difference in the socially acceptable exhibitionistic behavior of women in that something is accomplished, a natural goal is obtained, while the form of exhibitionism under discussion is a bizarre type of behavior and nothing is attained except apprehension and punishment. The cases on which Dr. Falstein reported from the Institute for Juvenile Research are certainly of importance, and long term studies should be made on them together with studies similar to this so that one may get an idea whether this behavior represents an adolescent experience, which in our opinion it does not, or whether it starts at some later time. I have an idea that it starts very early, but whether it can be prevented from continuing into older age groups is something about which nothing is known. I was surprised that the literature is so barren of any detailed case reports and evaluations of psychotherapy.

Effect of Emotional Excitement on the Insulin Content of the Blood: Contribution to Physiology of the Psychoses. Drs. E. Gellhorn, J. Feldman and A. Allen, Chicago.

This article appeared in the February 1942 issue of the Archives, page 234.

DISCUSSION

Dr. David Slight, Chicago: The physiology of the emotions is a topic of great interest and obvious importance in psychiatry. Time is short to do full justice to a discussion of Dr. Gellhorn's interesting paper, but I shall raise a few questions.

All psychiatrists should be interested in fostering research by physiologists, biochemists and other research workers in the problems of psychiatry. However, it is necessary to establish definite standards of clinical diagnosis, so that in the correlations of the biochemical and other laboratory findings and the clinical conditions one can be assured of their validity. Thus, to speak of the chemistry or the physiology of the psychoses is like speaking of the chemistry or physiology of any heterogeneous group, such as a political party or a social group. The psychoses comprise a variety of disorders that differ in clinical and, in some cases, physiologic and pathologic characteristics. With the present studies in mind, one recalls that in part of the manic-depressive psychoses changes in carbohydrate and lipoid metabolism appear, as I helped to show some years ago. Obviously, such psychoses stand apart from others of the same clinical type and from other clinical types. There is little justification for grouping the psychoses as an entity for purposes of physiologic or biochemical research.

In regard to the controls, I should like to know the number of normal subjects; it seemed from the lantern slides there were only 6. All know the difficulty of experimentally producing emotion in the human being; experimental psychologists have long been confounded with this difficulty. As to the normal controls, it is doubtful whether after an examination in physiology, which I gather was the "stimulus," emotional excitement would be comparable to the emotional excitement of psychotic patients. There may have been some similarity in the emotional excitement before the examination, but after it the students were more likely to be fatigued or emotionally "exhausted." I should like to hear Dr. Gellhorn speak with regard to this point.

Dr. Gellhorn spoke in passing of sham rage, and I believe he said that he obtained the same results in animals with sham rage as in animals with ordinary emotional excitement. Then he said that various workers have doubted whether the emotional expressions of hysterical persons had the same physiologic basis as the emotions of normal persons. Certainly, hysterical persons may show facial and other external evidence of apparent emotion without evidence of organic reverberation, as indicated by absence of cutaneous change in response to the galvanic current and other indications of visceral change—that is, mimetic emotion. However, that kind of sham emotion, if one can call it so, is not comparable to what is called sham rage in animals, if I understand Dr. Gellhorn to make such a comparison.

This is an interesting study, and it is to be hoped the work will be extended by Dr. Gellhorn and that other investigators will see fit to repeat the experiments. However, I can only emphasize that in all the many welcome research efforts in psychiatry being made by biochemists, physiologists and the like one should endeavor to make a careful differentiation of the clinical material. Diagnosis of the so-called functional psychoses, for example, is often difficult, but within the scope of clinical evaluation one should try to approximate as closely as possible to the standards of the physiologic or other test methods being used. Whatever the limitations of psychiatric nosology, one can at least refine the classification and clinical differentiation further than merely by talking of the psychoses.

Dr. M. K. Horwitt, Elgin, Ill.: For the past few months my associates and I have made an attempt to repeat this procedure on adrenodemedullated-hypophy-

sectomized rats, but we have not yet been able to duplicate the results reported. Our efforts have been confined to the standardization of the technic of assay using pure insulin, and we have not felt that the constancy of our results with this method were such that it would have been profitable to proceed to a study of the blood of patients with such a technic. Most workers take the microdextrose methods for granted, but on close analysis one will find that accuracy of the results is not greater than 10 per cent. This is especially true when small amounts of blood from the tail of a single rat are used in testing. It is our intention to continue our work on this problem in the hope that it may be possible to duplicate the data which Dr. Gellhorn has reported. It is even possible that the rats which we have been using have less sensitivity to insulin than those which Dr. Gellhorn used. The possibility of such a difference has been mentioned in the literature.

I should like to raise one question. In a paper published by Dr. Gellhorn in April 1941 it was indicated that there was enough insulin in the blood of an excited schizophrenic patient to cause a drop in the blood sugar of more than 25 mg. per hundred cubic centimeters in an adrenodemedullated-hypophysectomized rat. This drop, when translated from the curve of the assay which has been presented, represents approximately 0.001 unit of insulin. If it is assumed that the patient has 5 liters of blood, this means that 5 units of insulin are present in the blood of an excited patient at a given time. This is about five times the amount which Dr. Gellhorn has calculated for the normal person; that is, there is five times the normal amount of insulin in the so-called excited state. Dr. Sidney Klow and I have shown that 5 units given intravenously to a patient produces a drop in the dextrose content of the blood of about 30 to 40 mg. per hundred cubic centimeters in thirty minutes. How can one explain the presence of that much insulin in the blood of the excited patient without any change in the dextrose content? If the insulin is handled differently by the excited patient, why should not the addition of more insulin give an insulin tolerance curve which differs from the normal? Furthermore, if a patient has 5 units of insulin in his blood he would use dextrose at a tremendous rate to a point at which his metabolism would be markedly different from one supposedly normal, a condition which has not been observed.

DR. ERNST GELLHORN, Chicago: I agree with Dr. Slight that it would be important to perform systematic studies on the insulin content of the blood in different mental diseases. So far we have found no difference between the insulin content of the blood of schizophrenic patients and that of normal persons. However, general excitement causes predominantly a discharge of insulin in patients with mental diseases, indicating an abnormal balance in the autonomic centers, since normal persons produce predominantly a discharge of epinephrine.

Thus far our investigations have given no indication that the reaction is specific for a particular form of mental disease. The investigators suggest rather that various forms of mental disease are accompanied by a disturbance in the balance of the centers of the sympatheticoadrenal and vagoinsulin systems.

I admit that our control group is small, but it is exceedingly difficult to produce conditions which will give decisive emotional effects in normal persons. Moreover, the experiments on normal and on psychotic subjects indicate fundamentally different reactions.

Dr. Slight mentioned the distinction between sham rage and excitation. I do not think I have made any statement minimizing the essential differences between these two conditions. What I have emphasized is the fact that in both conditions the changes brought about in regard to the autonomic system are identical.

I cannot understand how Dr. Horwitt can make any statement with regard to our method of insulin assay, which he obviously has not used as yet. His assistant, Dr. Simon, told me that on injection of sodium chloride into hypophysectomized rats she had obtained variable changes in blood sugar, and she apparently agreed with me that she obviously had not yet learned the method of assaying blood sugar satisfactorily.

Clinical Significance of Insulin Inhibition by Blood of Schizophrenic Patients. DR. MARTIN G. GOLDNER, Chicago.

In view of experiments indicating that the anti-insulin effect of blood of schizophrenic patients is a characteristic biochemical disturbance in this emotional disorder (Meduna, Gerty and Urse), the problem of insulin inhibition and anti-insulin factors is discussed. The term insulin inhibition is defined, and the methods for its estimation, the technics, the difficulties and the necessary controls, are described. The literature on insulin inhibition by body substances, especially by the blood, is summarized, and experiments with blood of schizophrenic patients and with blood of normal control persons are reported on. An attempt is made to demonstrate the mechanism of insulin inhibition by blood as a ferment process. From both the literature and these experiments the following conclusion is reached.

Since moderate insulin inhibition by normal blood has been reported by several authors, this phenomenon cannot have significance for a particular disease. Insulin inhibition in a higher degree has been observed occasionally in blood of patients with insulin-resistant diabetes and seems to be related to insulin resistance. Insulin resistance, however, is rare in schizophrenic patients. Finally, the control experiments show that the inhibiting power of blood of schizophrenic patients does not differ significantly from the inhibition exerted by blood of normal persons, though both groups show a higher degree of insulin inhibition with Meduna's method than was found previously with other methods. The reaction, therefore, has no clinical (diagnostic or etiologic) significance for schizophrenia.

DISCUSSION

DR. HENRY T. RICKETTS, Chicago: Dr. Goldner has clearly shown that there is little difference between the blood of the schizophrenic patient and that of a normal subject with respect to ability to inhibit the action of injected insulin when the rabbit method is used. It is unfortunate, in a way, that this is so, for the proved physiologic abnormalities in schizophrenia are discouragingly few. I merely want to reenforce Dr. Ivy's remarks about the use of biologic methods in general. As I recall the paper to which Dr. Goldner referred, which purported to show that the blood of schizophrenic patients would prevent the hypoglycemic action of insulin, the authors used only 1 rabbit for each patient. Contrast with this, if you will, the practice of the Insulin Committee of the University of Toronto, which, when asked to assay the potency of a given batch of insulin on which my associates and I were working, sent us blood sugar curves obtained on rabbits in which each point on each curve represented the average of blood sugar determinations on from 55 to 82 animals. This is biologic assay as it ought to be made. Obviously, the committee used this large number of animals because of the large variations in the level of the blood sugar from one rabbit to another. If now one complicates the picture by introducing into it still another variable, the blood of the schizophrenic patient, how many more animals must one use in order to insure validity in the results? I would raise the question whether it is possible to demonstrate small degrees of insulin inhibition by the rabbit method. The use of this method has been reported by a number of investigators in an effort to find an insulin-inhibiting substance in the blood of diabetic patients who were resistant to this hormone. These attempts have been successful in only a small number of cases. Dr. Goldner and I have performed similar experiments on 4 insulin-resistant diabetic patients, requiring from 300 to 1,600 units of insulin per day. In 3 of these we were unable to find any such substance in the blood, and in the fourth the evidence was questionable. Since it has been impossible for us, and many others to demonstrate such an agent in frankly resistant diabetic persons, I can have only the greatest admiration for the courage of any one who attempts to find it in the blood of an ordinary schizophrenic patient.

DR. L. J. MEDUNA, Chicago: In collaboration with Dr. Gerty and Dr. Urse I studied 52 schizophrenic patients; so each point on our curves corresponds to

52 blood sugar determinations. We believe that this number is enough for plotting an average curve. The fact that Dr. Goldner did not find the same difference between the "normal" and the "schizophrenic" curves is probably due to some difference between his technic and ours.

DR. MARTIN G. GOLDNER, Chicago: The increase in the doses of insulin required to produce shock which is sometimes observed during the insulin shock treatment of schizophrenia seems to be due to changes in the insulin sensitivity rather than to insulin resistance. Such variations are frequently observed during the first period of insulin treatment; they seem to be of allergic nature and can be overcome by desensitization.

Regular Meeting, Nov. 6, 1941

Treatment of Psychotic Patients in General Hospitals and Sanatoriums.
DR. JACK WEINBERG and DR. H. H. GOLDSTEIN, Chicago.

A statistical survey of general hospitals and sanatoriums in the Chicago area revealed that 60 hospitals (representing 58.2 per cent of the replies received) treated 1,598 psychotic patients during the year 1940. The same group of hospitals admitted 582 psychotic patients during the year 1935. Modern methods of shock and chemotherapy were used with most of these patients. The staffs of most of the hospitals expressed the belief that the increase in admissions of such patients to general hospitals was due to the employment of shock therapies. The implications drawn from the statistical study were: (1) that many patients benefited from these treatments, though they were not given credit; (2) that an appreciable error is creeping into the statistical reports on the incidence of mental illness in the United States, for the cases of patients treated in general hospitals which do not have psychiatric units are seldom reported, and (3) that the trend toward treatment of patients in general hospitals is a healthy one. It obviates the stigma for the patient and his family; it lightens the burden on state-controlled institutions, and it leads to a better understanding among general practitioners and hospital staffs of the psychoses and psychiatric patients. This is of inestimable educational value in that it will hasten the public acceptance of the psychotic patient as a sick person for whom there is some hope of recovery or return to an acceptable community life.

DISCUSSION

DR. ROY R. GRINKER, Chicago: Dr. Weinberg's presentation is of great interest at a time when statistics emanating from mental disease hospitals are particularly confusing and distracting to psychiatrists attempting to orient themselves in regard to new methods of treatment. Before discussing his paper, I should like to inform you that his interest in comparing the fate of patients in mental disease hospitals with those outside is related to his new and serious responsibility. Dr. Weinberg is in charge of the new clinic in the Chicago area to which will be sent patients paroled and discharged from the state hospitals to that area. Through follow-up care, supervision of social service efforts and continued psychotherapy, his clinic will be able to evaluate the long term result of specific therapies as a needed part of research, and, it is hoped, will function effectively in decreasing the number of readmissions to the state hospitals. The Illinois Mental Hygiene Society and its committee which initiated the measures that made this clinic possible are pleased with the choice of Dr. Weinberg as its first director.

I should like, first, to indicate certain minor disagreements with Dr. Weinberg's statements. He speaks of convulsive shock treatment and chemotherapy as nonpsychiatric approaches to treatment, whereas he means nonpsychologic. One must not fall into the error of assuming that all therapy in psychiatry must be psychotherapy or some variation of that concept. Measures directed toward changing the internal environment of the body, whether of the blood, the cerebrospinal fluid

or the brain tissue, may in some instances be effective psychiatric therapy. Psychiatrists stand in a dangerous position if they lay themselves open to the accusation of being as biased as the so-called organicists.

Dr. Weinberg indicates that the recent trend in chemotherapy was responsible for the establishment of the two psychiatric units now operating in Michael Reese and St. Luke's hospitals. I cannot speak for St. Luke's, but I can for the Michael Reese and Billings hospitals. The psychiatric unit in the latter was really the first in a general hospital in Chicago and one of the first in the country. When I planned and operated the unit in Billings Hospital in 1935 and 1936 there was no thought that shock therapy would be used as it is today. The same holds true for the Michael Reese unit, which I planned in 1938 and opened in November 1939. That the result was an astonishing and overwhelming use of shock therapy is indicated by the fact that of the first 395 admitted patients at Michael Reese Hospital, 35 received metrazol, 35 insulin, 104 electric shock and 2 methylquinidine therapy, a total of 176 patients, or about 45 per cent. However, the actual reasons for establishing these units were several, chief of which was the desire to bring psychiatry into its rightful place in the field of medicine and psychiatric patients into the house of medicine, wherein all that medical science has to offer may be utilized in therapy and research, and in return to bring to the treatment of the medical patient a long-neglected psychiatric point of view.

In the questionnaire sent to the hospitals it was asked: "Was any form of the modern methods of treatment used on any of the patients?" and it was requested that the type be checked under the following headings: insulin, electric shock, *Dauerschlaf* and picrotoxin. All know Dr. Weinberg's intent in this question; yet how unfortunate to indicate that these methods constitute the modern armamentarium in psychiatric therapy! It is thus tacitly admitted that all the recently discovered dynamic etiologic factors in psychosomatic medicine are incapable of indicating a modern rational therapy.

Statistics regarding results in the shock therapies have been puzzling. In the first place, when comparison with spontaneous remissions was necessary it was found that preshock statistics were poorly organized and inadequate. The initial high rate of recovery or improvement after shock therapy of schizophrenia indicated that adequate scientific controls of the results had not been made. The cold, hard facts of reality have finally been allowed to come to light—that after a temporary lift, a brief remission, the end results were not much better than those which occur spontaneously. This was reported last year in Milwaukee. Now Dr. Weinberg feels that the present state hospital statistics reflect the fact that patients now referred to these institutions are more of the chronic, incurable type, the favorable ones having been successfully weeded out by early therapy in general hospitals. Let us see what actually has happened at the Michael Reese Hospital, where usually patients with the most favorable and early forms of the disease are treated.

From January to July 1940 no electric shock treatments were given; 30 patients (28 per cent) were given metrazol and 13 (12 per cent) insulin. From July through December 4 patients received metrazol and 49 electric shock treatments (37 per cent of all patients), and 13 patients (9 per cent) were given insulin. From January to June 1941 there were no metrazol treatments, and 55 patients (37 per cent) were given electric shock therapy. Nine patients (6 per cent) were treated with insulin. Thus, in this eighteen month period there was evidence that shock treatment of affective disorders, because of its beneficial results, increased in frequency. During the same period the use of insulin therapy of schizophrenia declined to 50 per cent of its initial frequency. This is in agreement with current opinion regarding its efficacy. Furthermore, among schizophrenic patients, regardless of the type of therapy used, the numbers of improved and of unimproved patients were about equal. Direct referrals from Michael Reese to the Psychopathic Hospital were approximately 8 in an eighteen month period.

These cases comprise a sampling of the middle class population of Chicago, and there is no reason to suppose that they are not representative and that the

complexion of the psychoses of other socioeconomic groups is different. If the results which my associates and I obtained were not good there is no reason to believe that results under state hospital supervision could have been better, since our conditions of operation are facilitated by greater funds for nursing and medical care and for special equipment. The few patients who were improved or whose disease was in remission could hardly alter the total percentage on which the state hospital statistics are based. Since our statistics are not in favor of insulin therapy, we cannot be accused of detracting from the good results indicated in their early tables.

I, therefore, do not agree with Dr. Weinberg that sanatoriums and private hospitals influence the results for state hospitals. I think the initial enthusiasm for nonpsychologic therapy of the psychoses loaded the early statistics in that results were uncontrolled, false remissions were included and poor diagnostic criteria were used. Now it is being shown that good scientific observations and sound statistical studies are placing the shock therapy of schizophrenia in the position it deserves—which in no wise minimizes its real value in certain selected cases under specific indications.

Dr. Ralph C. Hamill, Chicago: No insane person is 100 per cent insane, and all can respond to ordinary conditions to some extent. The punishment significance of shock therapy is something that cannot be disregarded. Last year at the meeting of the Central Neuropsychiatric Association, in Milwaukee, I spoke my mind on this subject, saying that Dr. Ziegler omitted to mention the form of shock therapy with which I was familiar in my five years at a hospital for the insane. A hunk of soap in a sock gives a shock. After I had got over the sense of mystery that insanity had for me, I began to realize that, after all, the insane were not insane all the time and that when a patient was hit with a hunk of soap in a sock he knew he had to behave. When a man in a quiet ward became disturbed he was sent to ward 4. Ward 4 had two burly, pug-ugly attendants. It was quiet. At first I was puzzled by the fact that an acutely disturbed man would very quickly quiet down in this ward. It was not until I had become thoroughly acquainted with the hospital that I began to hear of the soap in the sock; then I began to connect the pug-ugly attendants and the improved behavior with this rumor. The soap in the sock shocked the offender into good behavior, and the appearance of the attendants kept the threat hanging over him. That's something that cannot be disregarded. It's the same situation as that of the enuretic patient who gives up urinating in his bed after being given 5 grains of sodium bicarbonate. He may think that it is the medicine that makes him quiet. Such a mechanism may be all important in shock therapy. The insane take advantage of the fact that they are insane. They burst out with the most outrageous profanity, urinate on the floor and otherwise act outrageously to show they are really insane. After treatment with the soap in the sock they behave. I don't know but that that is a practical shock therapy. We blind ourselves with the worship of the mysterious instead of seeing the actual physical facts.

Dr. C. S. Sommer, Chicago: The discussants have been so concerned with Dr. Weinberg's remark on shock therapy that attention has been distracted from his central theme, namely, that there has been a large increase in the number of psychotic patients treated in general hospitals. I think there might eventually be some diminution of state hospital work, owing to the fact that general hospitals are giving attention to and taking care of patients with early mental disease, whether shock therapy is efficacious or not. At least these patients with early disease are being treated. The idea that Dr. Weinberg has brought out, namely, that general hospitals can be helpful in the mental illness problem, offers support to the idea that state hospitals can turn back to the general practitioner, and especially to the private practitioner of psychiatry, some of the responsibiliy that they have carried in the past, whether this be the care of patients who have never been in a state hospital or the supervision of paroled patients. One of the tasks of Dr. Weinberg's clinic will be to see whether the number of commitments can

be reduced by referring to the psychiatrist or to the family physician some of the patients who are on the verge of being committed. Advice and guidance from those who are in private practice will be needed in undertaking this new phase of his program in the wisest possible way. This may seem to be a swing away from state medicine and a return to private practice. Since so often one must perforce undertake enlarged programs of state medicine, one welcomes a balancing opportunity to turn patients back to private practice and general hospitals.

DR. JACK WEINBERG, Chicago: I am extremely grateful to Dr. Grinker for his remarks and for his thoughtful discussion. I agree with him that I probably should have used the term "nonpsychologic" rather than "nonpsychiatric." I hastily corrected myself when I wrote modern methods with reference to metrazol and other shock methods. I meant shock therapy, not all the methods psychiatrists have employed in the treatment of psychotic patients. It is precisely because I had wished to get at the results for these patients who are being treated in the hospitals that I undertook this survey. I wanted to know how many of the patients who are being treated are receiving help and, if not, why they are being treated. It has always been a mystery to me why any psychiatrist who feels that shock therapy is of no use will still send a patient to an institution where he knows some form of shock therapy will be given. I see that the results of St. Luke's and Michael Reese hospitals are in agreement in that few recoveries are produced; therefore, the drop in reported good results in the state hospitals must be due to a declining enthusiasm for the treatments.

I must, however, disagree with Dr. Grinker on the question of insulin shock therapy. I am convinced that this form of treatment is unsuccessful in the general hospital because of its manner of application. Insulin shock treatment is not to be relegated to the intern or the resident, who merely supervises the therapy. The success of the treatment depends a great deal on the interest of the psychiatrist who uses the helplessness, the extreme dependence of the patient at the termination of the coma to establish a transference and good rapport with him. The exploitation of this situation is invaluable and has, to my mind, been a great factor in the consistently good results that I have had with hypoglycemic therapy at the Chicago State Hospital.

That shock therapy serves as punishment, and thus psychologically alleviates many a mental disorder, may be true in some cases. In many of the involutional psychoses and in the depressive affective psychoses in which the patient will inflict punishment on himself shock therapy may be looked on as another form of punishment and be accepted. I am not so sure whether punishment per se ever alleviated any severe mental disorder. In many other patients, particularly when insulin therapy is employed, there are, as Dr. Grinker stated, many changes in the blood chemistry and physiology that might produce effective results.

I also wish to thank Dr. Sommer, who has again brought to mind the point in which I was interested, namely, that the manifest trend toward the care of psychotic patients in general hospitals is going to be of great value not only to the patient but to the acceptance of the treatment of the psychotic patient as a matter of course in a general hospital, and away from special institutions.

Personality Factors in Thyrotoxicosis. DR. JOSEPH C. RHEINGOLD, Chicago.

A six year experience as psychiatric consultant to the thyroid clinic of the Michael Reese Hospital and the special study of 144 thyrotoxic patients have led to the view that thyrotoxicosis is a series of total organism reactions, with limitless variety in the symptom complex, and represents failure of adaptation, governed by inherent vulnerability, to any, and usually many environmental demands. The constitutional vulnerability factor has been variously defined as a "degenerative anlage," a distinctive constitutional type—Graves's constitution—or the autonomic lability of the leptosomic person. In the cases reported, every morphologic type is represented, although the leptosomic predominates, and while some subjects appear to have a stable constitution, evidence of what von Bergman called "vege-

tative stigmatization" is the rule. Similarly, the personality varies from the occasional stolid temperament to the rather common sensitive and emotional type. Descriptions in the literature on the premorbid personality are apparently colored by the behavior change induced by the disease, for although the nervousness of the thyrotoxic patient is sometimes but an exaggeration of his characteristic behavior, it is not uncommon to observe reversal of behavior tendencies, which the patient regards as a compulsive transformation. The attempt to isolate a circumscribed emotional situation as specifically related to the genesis of the disease has produced as many alleged specific causes as there are writers on the subject. In the present series of cases none of the reported psychic conflicts occurred frequently enough to warrant special grouping. Other types of conflict situations were found. The relevance of a given conflict situation to the genesis of the disease is always open to question. In some instances the development of thyrotoxicosis is inseparable from the emotional life of the patient; in others the disease appears to be entirely independent of the personality.

An acute emotional experience is held by most writers to be the usual precipitating event. The percentage of patients who spontaneously declare that the disease was initiated by an emotional crisis is larger than in the case of any other disease, and systematic inquiry frequently discloses a temporal connection between a personal experience and the appearance of symptoms which were not recognized or had been repressed by the patient. But the reported or elicited emotional situation may be merely coincidental with the onset of the disease or a parallel phenomenon, or it may have occurred after the disease was established. In clinic practice one is more impressed by the influence of the cumulative stress of trying life situations. In some cases a nonpersonal event, such as an operation or infection, appears to have been the releasing influence. In general, one may say that any environmental stimulus that makes demand on the autonomic system creates the stress which precipitates the disease in the predisposed person.

Classic exophthalmic goiter is probably the end stage of a morbid process that has its inception in an anxiety state or autonomic imbalance. Diagnostic differentiation is difficult. Insight is gained by discarding nosologic arrangements and reviewing this syndrome as a total organism reaction with a unique constellation of determinants and clinical manifestations in the individual case. Although the association of a psychosis with thyrotoxicosis is rare, a fundamental problem is created by the relative frequency of manic-depressive states and the virtual absence of schizophrenia.

The variability of causes and of clinical expressions dictates an elastic program of treatment. The preexophthalmic goiter syndromes require medical and psychiatric management. When thyrotoxicosis is established, thyroidectomy is indicated as the most efficacious remedy. At least three fourths of the patients attain symptomatic cures, and of these about one-half report a personality change, usually described as a rebirth. In the present series, 16 patients have continued to exhibit this improvement on the premorbid personality for from two to five years after operation. Poorly integrated persons seldom show lasting personality change and become thyrotoxic again or show visceral neuroses or psychoneuroses. In these cases thyroidectomy is to be regarded as palliative; curative therapy is psychiatric. Failure of thyroidectomy is correlated not with any feature of the disease but with a vulnerable constitution as expressed in autonomic disorders in the family and in the patient prior to the onset of thyrotoxicosis. Such unstable persons are usually not helped by any form of treatment.

DISCUSSION

DR. THERESE F. BENEDEK, Chicago: Dr. Rheingold's paper is an excellent presentation of a great variety of problems which are involved in the process of thyrotoxicosis. He has put me in a difficult position, since it is not easy to discuss a paper with which one agrees. I should emphasize our agreement in that thyrotoxicosis is the most impressive clinical syndrome of psychosomatic processes; he correctly stated that the literature reveals that the cause "is specific

not for the disease but for the patient." This indicates, however, that the study of this condition has brought but little insight into the interrelations of those psychic and somatic processes which are diagnosed as thyrotoxicosis. The reason for this may be sought in the fact that students of these problems belong to different schools of thought and approach the problem from different points of view. Psychosomatic medicine, although it was the aborigine of medicine, had to be rediscovered, and its scientific merits have been established only in recent years. Psychosomatic medicine is a young science. Its workers, it seems to me, still apologize for their scientific beliefs or findings. One seems to apologize because his point of view is "too psychologic"; the other, because it is "too biologic." A more comprehensive understanding can, however, be expected only when more cases are completely studied from both points of view.

My purpose is, of course, only to define what I mean by complete study of a case from the psychiatric point of view. I divide this study practically into three parts: The first is the study of the premorbid personality. By this I understand the possibly complete study of the development of the patient, the psychodynamic structure of his personality, the structure and meaning of his symptoms, etc. The second part is the investigation of the traumatic situation, if it was such, or, in general, the study of the period during which the thyrotoxicosis developed. The third is the study of the psychodynamics of the emotional conditions and symptoms during the dysfunction itself.

During the upset, and almost desperate, emotional state of a person in the acute stage of thyrotoxicosis, one hardly can get the material for the first part which I mentioned. In this state the patient is full of anxiety or is actually psychotic; thus the information which is obtained falls into the third category. One can study the material which might reveal the psychogenesis only later. Such a complete study of a case, however, might reveal that the patient's development, and his premorbid personality, already determine what might or did constitute a psychic trauma for him. Only such a study might create order in the great variety of "psychic traumas" which are mentioned in the literature. Psychoanalytic study of the cases shows that a situation becomes traumatic for a person when it is apt to mobilize conflicts and anxiety already prepared by his previous development. When the case is studied from the point of view of the total personality, one will recognize that the content of the emotional difficulties during the thyrotoxicosis—although disturbed and aggravated—have a direct causal connection with the conflicts of the premorbid personality. Still, this does not mean that the psychologic content, or the causative dynamic factors, of a thyrotoxicosis are correctly described, as in the cases cited by Dr. Rheingold in his paper. Although those examples, chosen to demonstrate that psychoanalysts believe that "father impregnation fantasy materialized in thyroid," or "that the mystery of a half-swallowed child" is what caused the goiter, were selected from an earlier phase of psychoanalysis, in which one was inclined to believe that fantasies might have a symbolic expression in the organic symptom, the citations of Rheingold do not do justice even to the psychoanalytic concept of that early period. The earliest concepts of psychoanalysis emphasized the organic origin of anxiety, and its main thesis was that anxiety is the motor of every neurotic symptom. When the examples cited by Rheingold are considered from this dynamic point of view, one recognizes that those fantasies are not primary causes but elaborations of the anxiety, which is the main symptom of thyrotoxicosis.

To tell the truth, one is not much closer to the understanding of the pathologic processes of the thyrotoxicosis. The source of anxiety in the thyrotoxicosis cannot be easily determined. If there was a primary emotional process, a neurosis, which sustained anxiety and hostility, these emotional processes could not be separated from the accompanying changes in the endocrine system. In the same way, if the endocrine imbalance is the primary factor and sustains an emotional tension, this might be warded off for a long time by means of the ego function. Rheingold cited an interesting description by Moschcowitz of the premorbid per-

sonality of thyrotoxicosis—a perfect description of a person who defends himself against anxiety by a narcissistic oversensitiveness. If this defense breaks down, as a result either of psychic trauma or of purely somatic increase of the thyroid function, it will be washed away and only a helpless abandonment to anxiety remains. It is the task of the psychic apparatus to bind anxiety. Some years ago, in studying 2 cases, I described the psychodynamic processes as they developed as a defense against anxiety in thyrotoxic states. It would be too tiresome to cite these examples in detail. It was shown that the content of the psychic symptoms in thyrotoxicosis cannot be anything else but phobia, a projection of the anxiety or depression, since helpless ego cannot protect itself against anxiety in any other way than by self punishment. I hope that further study will reveal the intricate interrelation of the psychic and somatic processes.

DR. JOSEPH C. RHEINGOLD, Chicago: I am grateful to Dr. Benedek for enlarging on an aspect of the total problem. In some patients the personality seems intimately bound up with the origin and the course of the disorder. In working with these patients one tends to forget that they are suffering from thyrotoxicosis; one treats them as neurotic subjects. The whole life experience, the psychic conflicts and the emotional situation at the time of the onset of the disorder enter significantly into the formulation of the case. But this type is not the rule in cases of thyrotoxicosis. Even intensive study fails to bring out a convincing personality-disease connection in some instances. I interviewed several subjects fifty times or more over a period of two, three or four years without discovering adequate explanation of the disease in the personal material. All that one is warranted in saying is that as far as the participation of personality is concerned the range of variation is from the case in which nonpersonal factors seem prepotent to the case in which one is dealing essentially with a neurotic disorder. Rather than try to find a perspective which best describes all of these patients and lends itself to a standard therapeutic approach, I have sought to appraise all the factors in the etiologic constellation in the individual case and to allow this analysis to suggest the plan of therapy. I take no sides. Although I agree with Dr. Benedek that the insight of the psychoanalyst is essential to a proper understanding of thyrotoxic patients by and large, I believe that the insights of the physiologist, the pathologist and the chemist are just as relevant. It is only when one brings these insights together and achieves a biologic point of view that one's understanding of thyrotoxicosis is fitted to all the facts.

Clinical Experience with Beta Erythroidine Hydrochloride in Metrazol Shock. DR. WILBUR R. MILLER, Iowa City.

At the Iowa State Psychopathic Hospital my associates and I found that the use of metrazol in the treatment of depressions was accompanied by undesirable effects, chief among which was the danger of fractures and dislocations. In addition, the apprehension and fright of the patient preceding the treatment were considered therapeutically detrimental and made the administration of drugs sometimes difficult. The experience of Rosen, Cameron and Ziegler with beta erythroidine hydrochloride at the Albany Hospital indicated that this drug, with its curare-like effect, should be given further clinical trial. Since the drug was produced in pure form and could be easily standardized, it had advantages over other curare-like products. It was given in a 10 per cent sterile, filtered solution at the rate of from 2 to 4 cc. a minute until change in the pupils, dysarthria and weakness of the muscles were perceived. Immediately after the injection metrazol was given as usual, resulting in a convulsion with marked diminution of the strength of the movements.

A group of 47 patients were given the drug, the majority of whom had depressions of either the involutional or the manic-depressive type. A total of 251 treatments were given, only 1 of which resulted in a fracture which was confirmed roentgenographically. This fracture, however, was not clear enough to warrant any special treatment, and the use of metrazol was not discontinued. Fourteen

patients, with a total of 32 treatments, required the use of prostigmine as an antidote to the beta erythroidine. Artificial respiration was resorted to three times. Treatment of one patient was discontinued because of sensitivity to the drug.

A follow-up study of the patients made since discharge showed that the use of beta erythroidine hydrochloride does not interfere with the therapeutic effects of metrazol.

In conclusion, beta erythroidine hydrochloride is considered a distinct aid and protection to the patient who is receiving metrazol convulsions, protecting him from fractures and dislocations. However, no change was noted in the apprehensiveness and fear preceding treatment. No fatalities occurred, although the administration had to be watched carefully. Antidotes had to be on hand to counteract any undesirable effects of too great a reaction to the drug.

DISCUSSION

DR. NORMAN A. LEVY, Chicago: The problem of skeletal injuries resulting from convulsive shock therapy is of the utmost importance to the practicing psychiatrist, as one of the main tenets of the hippocratic oath is that the physician's treatment not harm the patient. Dr. Miller, following the procedure described by Rosen, Cameron and Zeigler (The Prevention of Metrazol Fractures by Beta-Erythroidin Hydrochloride, *Psychiatric Quart.* **14**-477, 1940), has demonstrated that beta erythroidine hydrochloride, a drug with a curare-like effect on the myoneural function, reduces the intensity of the convulsive seizure and minimizes the occurrence of fractures and dislocations. It is of interest to note in passing that this drug was first utilized clinically by Burman (Therapeutic Use of Curare and Erythroidine Hydrochloride for Spastic and Dystonic States, ARCH. NEUROL. & PSYCHIAT. **41**:307 [Feb.] 1939) in the treatment of spasticity and dystonia. Burman also used curare first and then experimented with erythroidine because it was considerably less toxic, although less effective than curare. In consideration of the fairly high incidence of skeletal injuries associated with metrazol convulsive shock therapy, this procedure obviously has much to commend it. I am glad that Dr. Miller mentioned the sometimes serious toxic effects and the necessity for careful observation of the patient and the ready use of counteracting remedies, especially prostigmine and other life-saving measures. Idiosyncrasy to the drug seems to occur, with severe circulatory and respiratory symptoms, as emphasized in a recent article by Rosen and Borenstein (The Psycho-Physiological Action of Beta-Erythroidin Hydrochloride, *Psychiatric Quart.* **15**:163, 1941), so that it must be used with caution, especially for older patients, in whom cardiovascular disease is always a possibility. The 1 death which my associates and I have had after an electrically induced convulsion occurred in a man who had been given curare. He died of acute myocardial failure, and autopsy revealed the presence of coronary sclerosis. Dr. Miller reports a severe reaction in a man of 47 and states that the older patients tolerated the drug less well. I should like to ask Dr. Miller to what extent serious circulatory and respiratory difficulties appeared in his patients, especially the older ones.

Inasmuch as we gave up the use of metrazol a year and a half ago, we have had no first hand experience with this drug. Our experience evidently agrees with Dr. Miller's that convulsions induced electrically are less severe than those induced by metrazol and that minimization of the seizure by drugs is unnecessary. It might be opportune at this time briefly to summarize our experiences with skeletal injuries during electric shock therapy at the Michael Reese Hospital. During the past year vertebral fracture has occurred in 3 patients, chip fracture of the humerus in 4 and dislocation of the jaw in 2. Roentgenograms of the spine were obtained only in the patients complaining of persistent pain in the back, so that the actual incidence of asymptomatic vertebral fracture is not known. The chip fractures of the humerus occurred in elderly persons with osteoporotic bones. Whether or not these accidents could have been eliminated by the use of erythroidine cannot be stated, but the incidence is not sufficiently high to warrant the use

of a drug the toxic effect of which is not infrequently severe. In our experience the use of a Bradford frame and careful physical restraint of the patient during the seizure by those assisting in the treatment are of primary importance and usually suffice to prevent skeletal injuries.

DR. WILBUR R. MILLER, Chicago: In answer to Dr. Levy's question, we were rather cautious about the patients whom we treated. If they showed any signs of cardiac or respiratory disease, we did not give them shock treatments; so for the most part we eliminated the respiratory difficulties. On the other hand, we were bound to miss something, and the older patients, that is, those over 50, most frequently showed difficulties of respiration. I think, with the exception of the man who showed definite idiosyncrasy to erythroidine, that there was no bad reaction to metrazol among the younger patients. Metrazol treatment was not continued without erythroidine in his case because of the objections of the relatives, who removed him from the hospital.

NEW YORK NEUROLOGICAL SOCIETY AND NEW YORK ACADEMY OF MEDICINE, SECTION OF NEUROLOGY AND PSYCHIATRY

A. A. BRILL, M.D., *President of the New York Neurological Society, Presiding*

Joint Meeting, Oct. 7, 1941

Presidential Address. DR. A. A. BRILL.

The Electricfit in the Treatment of Mental Disease. DR. DAVID J. IMPASTATO (by invitation) and DR. RENATO ALMANSI (by invitation).

In 1938 Cerletti and Bini, of Rome, Italy, introduced "electroshock therapy." In 1940 we introduced this form of therapy in the United States. Because the term "electricshock" has obvious disadvantages, we have substituted "electricfit."

Patients best suited to receive this form of therapy are those suffering from functional mental disease. Some observers have used the method safely in a few cases of organic disease of the brain with psychosis. Others have extended the method to cure disturbances of sleep in morphine addiction, mental deficiency and alcoholism. It is now also being employed in the treatment of severe psychoneurosis.

Before treatment complete physical, neurologic and mental examinations, a roentgenogram of the spine and an electrocardiogram should be obtained. To prevent fractures the treatment is best given on a surgical bed the foot of which is raised as high as possible. The patient's back is hyperextended over this and held down at the shoulders and hips. His arms should be held to his sides and his legs held together in adduction. In addition, with a mouth piece in place, his jaw should be held closed during the fit.

Our technic has been to administer two treatments a week until the patient recovers. However, Myerson has given treatments only in accordance with the response of the patient and stops therapy soon after the patient begins to improve. These patients later go on to full recovery. We have followed this technic in a few cases and found it favorable.

We have observed four responses to the electricfit: (1) the conscious reaction, in which the patient does not lose consciousness and remembers the treatment; (2) the blank response, in which the patient does not remember the treatment but shows no retrograde amnesia; (3) the petit mal response, in which the patient is unconscious and shows definite retrograde amnesia, and (4) the grand mal reaction, in which the following manifestations occur, in the order indicated: the initial flexor spasm, primary apnea, the tonic and clonic phases, secondary apnea and the

postconvulsive phenomena. The initial flexor spasm consists of a lightning flexor contraction of the entire body, usually starting in the head and neck and traveling to the upper and lower limbs. In most cases this reaction is instantaneous, the entire body relaxing after one contraction. The response is due to cortical stimulation and occurs only in convulsions induced electrically.

The grand mal attack may be immediate; that is, it may occur at once after the initial spasm, or it may be delayed, coming from one to ninety seconds after the spasm. It may also be complete, with all the muscles of the body taking part in the convulsion, or partial, the convulsion being limited to a few muscles, usually those of the eyes and face.

The partial grand mal attack appears to be the most desirable reaction; with it danger of fracture of the spine or limbs is avoided or no violent convulsive movement occurs. We have found in a limited number of cases that this reaction may be obtained by placing the patient on a regimen of phenobarbital, ¼ grain (0.016 Gm.), three times a day, or by administering sodium amytal, 3¾ grains (0.243 Gm.), a few minutes before the fit is induced. Sodium amytal is also useful in allaying anxiety and in making resistive patients more cooperative.

Since February 1940 we have treated 80 patients by the electricfit method. Of these, 50 have completed their treatment. The results are shown in the following tabulation:

Type of Illness	No. Patients		No. Recovered	No. Improved	No. Unimproved
Schizophrenia					
Paranoid	12		3	6	3
Catatonic	5	27	1	2	2
Hebephrenic	10		1	1	8
Manic-depressive psychosis					
Depressed	12		6	4	2
Manic	3		1	1	1
Involutional depression	5		0	1	4
Compulsion neurosis	3		1	2	0

For further analysis, we have divided the group with schizophrenia into patients with the acute (illness of less than six months), those with the subacute (illness of less than two years) and those with the chronic (illness of more than two years) form of the disease.

Of the group with acute schizophrenia (11), 4 recovered, 6 improved and 1 did not improve. Of the group with the subacute form (8), 1 recovered, 3 improved and 4 did not improve. Of the group with the chronic form (8), none improved. Thus it is seen that of the groups with acute and subacute schizophrenia, 77 per cent recovered or improved, while of the group with chronic disease none recovered or improved.

The only complications in our cases were dislocation of the jaw in 2 patients, a fracture of the fifth dorsal vertebra and a fracture of the scapula.

DISCUSSION

Dr. S. Bernard Wortis: One can only be impressed with the results which have been obtained by the electric shock treatment, and I think the authors are wise in being cautious about recommending its use for too many conditions. The things that may be said of the method are that it is easy to apply, it can be used with ambulatory patients, it is safe and controllable, in terms of hospital care it is less expensive, it does not produce fear and there are immediate unconsciousness and amnesia for the attack. It is of greatest help in the treatment of persons with depressions and involutional melancholia and of some with rigid psychoneurosis who are not amenable to psychotherapeutic help without such treatment. The statistics for the schizophrenic group certainly show that Dr. Impastato's experiences are as good as those obtained with metrazol or insulin, but the general experience of psychiatrists is to be less impressed with the results in the schizophrenic group.

Dr. Impastato has raised the question of fractures of the spine. Many of them can be avoided with proper care as regards the posture of the patient and with adequate help.

A word should be said about the effects of these various shock treatments on so-called brain metabolism. It has long been known that the brain uses sugar as a prime food, the other essentials being oxygen and enzymes. In spite of all the work that has been done in many research centers in the past four or five years, it must be said that the essential physiologic mechanism to which the beneficial changes induced by shock can be attributed are not known. It is wrong to say, as is too often done, that the common, or the essential, factor in shock treatment is the suspension of brain metabolism. There are many clinically unrelated neuropsychiatric conditions in which the total brain metabolism is diminished. This is true of acute alcoholism, mongolism and phenylpyruvic acid oligophrenia, and Cameron and his group have shown it is true for persons with cerebral arteriosclerosis who have a slow cerebral and total circulation time. Moreover, it should be remembered that the brain metabolism in persons with severe mental derangement may be normal. There is no gross change measurable in the oxygen metabolism of the schizophrenic patient, whether he has been successfully or unsuccessfully treated. Patients with dementia paralytica who show severe clinical changes exhibit no significant drop in brain metabolism. There are therefore necessarily other important factors to be studied in this treatment. In insulin shock the oxygen supply may be adequate and the patient cannot be brought out of coma unless he is given infusions of blood to supply other substances that may be essential for normal brain function. One must say, therefore, that the changes in brain metabolism that one sees in the schizophrenic patient are either of a magnitude not yet sufficiently great to be measured by present methods or are qualitative rather than quantitative.

Accordingly, one must say that undoubtedly other changes occur in shock treatment that are very important, and may be more important than the change in oxygen metabolism. Some of these may be alterations in the carbon dioxide metabolism, in adrenergic and cholinergic substances, in inorganic phosphates and in the total metabolism of the organism after shock treatment. Gjessing, of Oslo, Norway, found changes in the nitrogen metabolism which he claimed were significant.

Nevertheless, in summarizing all this work of the past few years, one must say that shock treatment is undoubtedly a help, whether the convulsions are induced by the electric current, by insulin or by metrazol or whether they follow nitrogen or carbon dioxide inhalation. This work has increased interest in and knowledge of mental disease and some of the pathophysiologic processes concerned with it. This also can be said of frontal lobotomy, whether or not one agrees with the validity of the procedure. Some conditions which are refractory to one shock method often are cured by another.

It has been suggested by many authors that there is needed a test to tell whether the treatment will be effective, and some workers (Harris, Horowitz and Milch and Gottlieb and Hope) have reported that the intravenous injection of sodium amytal in cases of schizophrenia is of prognostic value. Certainly, the work at the New York State Psychiatric Institute has shown that with intravenous injections of sodium amytal one can tell in a general way whether one will get good results by psychotherapeutic or physiologic methods of treatment. Patients who are not immediately cured may be made more amenable to psychotherapy. Many patients given only a few treatments will go on to a complete remission, as has been pointed out by the work of Myerson and of Impastato. Finally, let me emphasize that shock treatment is more effective and more beneficial to the patient when given in conjunction with psychotherapeutic help.

Dr. Benjamin Wiesel (by invitation): Dr. Kennedy and I have treated about 30 patients, of whom 20 had depressions. I should like first to say a word concerning the selection of cases. One patient we treated was a physician 72 years of age, who made a complete recovery. Another was a man in the fifties with

hypertension (blood pressure of 200 systolic and 100 diastolic) and many hemorrhages in the eyegrounds. He made a complete recovery after eight or nine treatments, with complete recession of the hemorrhages; it is now two months since his last treatment, and the degree of his hypertension is reduced by 10 mm.

As regards the position of the patient and its relation to fracture, I wonder whether the authors have always used the position illustrated in the picture. I ask because there is no evidence of restraint applied to the shoulders, pelvis or extremities. Fractures of the extremities can be eliminated, we believe, by restraint applied in the form of pressure on the shoulders and iliac crests while the extremities are gently restrained at the same time. This avoids the wild movements which might produce fractures of the extremities.

Of the 18 patients with true depression, 18 recovered. Thus far we have met with no complications. We are in agreement with the others that memory defects are only temporary.

Dr. Lothar B. Kalinowsky (by invitation): When, last year, Dr. Barrera, Dr. Horwitz and I gave here a preliminary report on electric shock treatment, we did not foresee the great enthusiasm with which this method would be taken up everywhere. However, reports on results are still scarce. Therefore it might be of interest to see Dr. Impastato's conclusions confirmed essentially by a study which was made possible for me with the large material at Pilgrim State Hospital. We selected 110 cases, representatives of the main psychotic syndromes, cases being preferred in which there was as little diagnostic doubt as possible to diminish the value of the conclusions. The decision as to discharge from the hospital was made exclusively by the clinical director of the Pilgrim State Hospital.

We distinguish the results thus: no improvement, improvement and remission. By using the term "remission," we tried to avoid the arbitrary distinction between "much improved" and "recovered," for "recovered" is an expression of doubtful value with respect to a disease in which one has no clue as to whether or not the patient will relapse.

In the groups of patients for whom convulsive treatment is considered specific, namely, those with manic-depressive psychosis and involutional depression, the results were convincing.

In the group of 10 patients with manic-depressive psychosis, depressed type, all had a full remission and are outside the hospital. Of 11 manic patients, 8 had a full remission, 1 was improved and 2 were unimproved. In the group with involutional depression, all the treated patients (10) are in full remission. Poor results were obtained with the paranoid patients with involutional psychoses. This group is probaby more closely related to the group with schizophrenia of late onset and therefore carries an unfavorable prognosis.

We are fully aware that the groups which are benefited most are those in which the majority of patients also have a spontaneous remission. Shock therapy, however, interrupts the psychosis at will and abbreviates the stay in the hospital or, when ambulatory treatment is given, may prevent hospitalization and commitment altogether.

The following types of schizophrenia are distinguished: illness of less than six months; illness of between six months and two years; illness of more than two years, and illness with previous remissions. Of 17 patients with illness of less than six months' duration, 14 had a full remission and 3 improved, so that all were benefited by the treatment. Of 19 patients with an illness of between six months and two years, 3 had a full remission and 8 improved. Of 20 patients with illness of more than two years' duration, none had a full remission and only 3 improved. Again, better results were obtained in a separate group of 14 patients with previous remissions, of whom, again, 4 had a full remission, 5 improved and only 5 did not improve.

It should be said that all the "unimproved" patients became at least quieter and more easily manageable. Therefore an additional group of 60 of the most destructive and assaultive patients with chronic disease were given three or four treatments, with the purely symptomatic aim of improving their behavior for at least a few weeks.

The difference between results in schizophrenia of short duration and the constant decrease of the remission rate when the disease is of longer duration cannot be stressed sufficiently. Early treatment is just as necessary in psychiatry as in other fields.

At this time it would be gratuitous to ask whether insulin or metrazol or electric shock gives the best results. It will be an important task for research in institutions to compare and eventually to combine the different methods. It would be a great mistake if institutions should give up insulin treatment. I wish to state here that several patients recorded here as unimproved or improved only by electric shock had a full remission after an additional course of insulin. The great progress of electric shock treatment, with its simplicity, should bring considerably more patients to early treatment than before.

DR. DAVID J. IMPASTATO: I wish to thank the discussers. I agree with Dr. Wortis' remarks.

The procedure we used to restrain patients was that shown on the first part of the film, where the patient on the surgical bed, with his spine hyperextended, is being held down by the shoulders and hips. The other scenes, in which the patients are not held, were taken for study. It is wise to have some one hold the legs and the arms to prevent fracture of the limbs.

Experience is often astonishing. At the beginning of this work we were chary of treating anybody with a systolic blood pressure above 140 to 150 mm. Tonight we have heard that Dr. Kennedy treated a patient with a systolic blood pressure above 200 mm. Dr. Myerson treated a patient with existing coronary thrombosis.

Treating patients with hypertension and coronary thrombosis should still be considered hazardous and avoided when possible. However, in selected cases in which the physician feels that the mental condition of the patient requires electricfit therapy, he may proceed with caution.

Dr. Kalinowsky's results corroborate ours. The electricfit can be considered of definite value in treatment of the acute schizophrenias.

Psychiatric Disorders in Forty Men Teachers. DR. EDWARD B. ALLEN (by invitation).

A study was made of the psychiatric diseases of 40 male teachers who were consecutively admitted to the New York Hospital, Westchester Division, between Jan. 1, 1936 and May 31, 1941—all being patients with whom I had personal contact.

The diagnoses were about equally divided between dementia praecox, manic-depressive psychoses and psychoneuroses. There was a miscellaneous group of persons with alcoholism, psychopathic states and involutional melancholia. The types of dementia praecox represented were catatonic and paranoid; the manic-depressive reactions were predominantly depressive and mixed, and the psychoneurotic types were anxious or depressed.

Numerical studies revealed that the teachers were relatively young on admission; 10 were in their twenties and 15 in their thirties. Five were the only children in their families. The 22 married teachers had a total of 25 children. Twenty-five teachers were temperate in the use of alcohol, and 7 were total abstainers. Fifteen had had previous attacks of mental illness. Sixteen had a history of previous hospital residence, but none had more than two. Two made suicidal attempts before coming to the hospital, and 1 made several attempts during his immediate residence in the hospital. Twenty-eight had relatives who had suffered from mental disease.

Twenty-one of the teachers were essentially introverted. This was associated with the fact that 14 were of athletic and 13 of asthenic habitus. Such findings were in keeping with their prepsychotic personality traits. Nineteen were seclusive, 10 unstable, 6 worrisome, 4 sensitive and 3 serious and overconscientious. Eight were egotistical, but only 2 were overactive. Many possessed a combination of these traits.

The teachers were of superior intelligence, so that exactly 50 per cent were able to return to their teaching duties. Their profession was in the nature of an

overcompensation for their instinctive and emotional limitations. In spite of this, they were more successful as teachers than they had been in their attempts at other professions to which they had aspired. Two partially sublimated their homosexuality in their teaching. None was recorded as expressing overt aggression toward his pupils, but he would release it in his home toward his wife or other members of his family. Many had a marked mother attachment and were jealous of their wives. Many became ill when faced with the decision for marriage. All the patients revealed some difficulty in psychosexual adjustment. They became ill because of their instinctive or emotional limitations rather than because of direct difficulty with their teaching duties. While many had differences with their superiors, nevertheless these disturbances were a reflection of previous inability to make an adjustment to their fathers.

Therapy consisted of first ruling out any physical pathologic condition and then determining whether or not the patient was capable of returning to teaching. If he was capable, he was helped to recognize how he had overcompensated in his teaching and was given instruction in how to accept his profession more in the nature of a satisfactory sublimation. If the patient was not capable, he was advised to accept his limitations gracefully and turn to less exacting tasks.

DISCUSSION

Dr. Edwin J. Doty (by invitation): Dr. Allen has presented a timely and interesting study of a particular occupational group, a group which is of great importance to society and therefore deserves the best therapeutic efforts and study of the medical profession. However, this group does not constitute a large proportion of admissions to a psychiatric hospital. In my experience at the Payne Whitney Clinic we have had 10 teachers out of 210 men admitted during the past three years. All were in the fourth or fifth decade of life, the average age being 49. From the diagnostic standpoint all had predominantly depressive illnesses, with 3 exceptions, 1 having depression with definite schizophrenic features, another evidence of cerebral arteriosclerosis and the third a psychoneurotic reaction showing anxiety and hypochondriasis. From the standpoint of personality makeup, these persons were quite comparable to the group reviewed by Dr. Allen. Outstanding were such traits as great conscientiousness, extreme meticulousness and insistence on high ethical standards. In keeping with Dr. Allen's observation, all the patients showed evidence of difficulty in sexual adjustment. A good many had difficulty in professional adjustment which was related to the psychopathology of aging. Many of them had trouble in handling the frustration of not obtaining the academic goals for which they had striven. Others had difficulty in adjusting to the competition offered by younger colleagues.

In regard to the outcome of the illness, 6 patients recovered and were able to resume their teaching. One of the remaining 4 patients had retired before his illness developed, and on recovery he resumed a rather inactive life, following some hobbies. The other 3 are at present under treatment in psychiatric hospitals.

Dr. Allen, in respecting time limitations, omitted a great deal of his discussion of the psychopathologic aspects. He presented 1 case in which he was able to bring out some of these features. In studies of such groups it is important to consider in detail the psychopathologic basis of the reactions, so as to develop leads that can be used in the treatment. Also, the psychopathologic features should be compared with those shown in the personality disorders of patients in other occupational groups of similar ages and backgrounds.

Dr. Allen spoke of shock therapy having been employed with 7 patients of his group, 3 of whom recovered. By "recovered" I presume he means they went back to their work and suffered no disturbances in thinking or difficulty in retention. I should like to have him express his opinion as to shock therapy in this particular occupational group, that is, whether he feels at all reluctant to use it, in view of the fact that a teacher has to go back to a profession where the highest type of intellectual efficiency is desirable.

DR. EMIL ALTMAN: I think I am here under false pretenses. I read Dr. Allen's manuscript, and I regret that time did not permit his giving the full content of his paper. It would be presumptuous of me to go into any phase of his paper regarding etiology or therapy. I wish simply to take up one point, the feasibility of teachers with psychiatric disturbance returning to teaching at any time. I have studied this matter for forty years, and I have yet to see a teacher who had been psychiatrically disturbed come back and be efficient, not because of the intellectual but because of the emotional requirements. He is never established on the status of the normal person. To begin with, such a teacher has never been normal. He has kept on in his position and has received a satisfactory rating, but a satisfactory rating by a principal or superintendent does not mean the teacher has done satisfactory work. I shall give an illustration of what a satisfactory rating by school officials means. In New York city there are 37,000 school teachers. When I came to the Department of Education perhaps 3, or at the most 4, teachers were rated as unsatisfactory. After the supervising staff was taken to task for what seemed to indicate careless rating, a maximum of 28 teachers was reported as unsatisfactory. When, again, supervisors were directly charged with shielding their inefficient teachers, within two months 250 teachers were rated as unsatisfactory. At some future time this organization should take on itself the task of studying this matter. Psychiatric disorders in teachers must be considered in relation to their occupation and to the possible effects of their behavior on the children entrusted to their care. In this connection it must never be forgotten, as Sprague has said, that the psychotic personality never changes. It has its different aspects, like the obverse and the reverse of a coin—there are periods of quiescence and periods of active psychotic manifestations—but essentially the personality is the same. This imposes a heavy responsibility on the medical profession. In spite of personal sympathies and our natural tendency to ally ourselves with the welfare of our patients, it is our duty as physicians to see that teachers with psychiatric disorders are kept out of the classroom and that the public is made aware of the unfitness of such persons for the guardianship of children's minds and emotions.

DR. EDWARD B. ALLEN: I should like to answer the question which Dr. Doty asked in regard to shock treatment: Is it a thing which should be advocated for teachers with a high intellectual level, in view of the question of their returning to teaching? The teachers whom we called "recovered" and who returned to their teaching are reported to have done better than before. There are a great many ways of interpreting such a remark. I do not say the patients are more capable than they were before; a good deal of wish fulfilment enters into that. Such statements are obtained from friends and relatives of the teachers and from the patients themselves, and it must be remembered that the majority of these patients were serious minded and their prevalent reaction was anxious or worried. It is known that when a patient gets over a depressive phase he is likely to react in the other direction and be somewhat overactive. All this must be kept in mind in interpreting these statements.

In regard to the question whether these teachers should return to their teaching: Ours was an unusual group. They were of superior intelligence, had made good in their teaching in the majority of instances, and were wanted back by their schools; a great many taught in private schools and colleges, and not in the public school system, and there was a desire to have them back. We left the question of whether they should return to the authorities of the school; we were neutral in our attitude and made no promises about the future. However, in a group as erudite as this one, it would seem that there would be instances in which the patient could go back to his teaching. It is true there are emotional problems that have to be considered in relation to the pupils. We do not know the reaction of the pupils. We know what the school authorities said, but we have no recorded instance that the teachers had in any way affected their pupils in an unfortunate direction; as far as we can ascertain, their work had been of value and they had been helpful to their pupils.

Book Reviews

The Modern Treatment of Syphilis. By Joseph Earle Moore, M.D., with the collaboration of Jarold E. Kemp, M.D.; Harry Eagle, M.D.; Paul Padget, M.D., and Mary Stewart Goodwin, M.D. Price $7. Pp. 674. Springfield, Ill.: Charles C. Thomas, Publisher, 1941.

This book is the second edition of Moore's "Modern Treatment of Syphilis." The first edition appeared in 1933. Although revisions and additions were made by the four collaborators, the book still fortunately bears the uniquely personal touch of its chief author, and none of its characteristic features has been abandoned. It shows not only the personal touch of the author but that of the Johns Hopkins syphilis division. The spirit and attitude of this division apparently are largely identical with the author's.

The book is a detailed description of current practices and results in the treatment of syphilis. Special reference to experiences gathered in the Johns Hopkins Clinic is made throughout the book, and on these experiences the book is based. The opinions and results of other authors and clinics, however, are not ignored, but are carefully reported, discussed and referred to.

The scope of the material used is tremendous—over 35,000 cases of syphilis within a span of thirty years. Extensive use has been made of contributions of the so-called Cooperative Clinic Group, composed of the chiefs of the syphilis clinics of several universities and of representatives of the United States Public Health Service. This wealth of material and observations, because of its magnitude, might easily have been more of a liability than an asset but for its admirable statistical evaluation. The consideration of the therapy of syphilis is complete; no detail, no therapeutic problem is overlooked, and the presentation is clear, simple and didactic. The most important facts are emphasized by being boxed.

The patient is a human being; his psychologic, social and financial situation, so important in syphilis, is by no means forgotten. Special suggestions how to discuss the disease, its prognosis and treatment, its marital and social implications, with the patient are given. This seems to be one of the outstanding features of the book. The mental reactions of the patient, for instance the "overtreatment syndrome," are described briefly but thoroughly. The relation of the expert to the practitioner is clearly outlined.

In treatment of early syphilis, Moore prefers arsphenamine to other arsenicals. Details as to the use of mapharsen are scattered throughout the book and form one of the eighteen major items introduced into the second edition. Moore feels that mapharsen or another arsenoxide may possibly take the place of arsphenamine in the treatment of early syphilis and of neoarsphenamine in the management of late syphilis.

Readers of this journal will be mainly interested in the broad chapters on neurosyphilis. The discussion of asymptomatic neurosyphilis and its relation to seroresistance and the discussion of the prognostic significance of the spinal fluid changes are of special interest. Moore shows that neurosyphilis is in part preventable. The 25 per cent expectancy in cases in which no treatment is given can be reduced to 5 per cent or less (routine spinal fluid studies; intensified chemotherapy; fever therapy).

All methods of fever treatment and their results are described, with malaria rightly considered to be superior to other methods in management of dementia paralytica. As to tryparsamide, it is noteworthy that in recent years "reactions formerly rarely if ever observed . . . are beginning, for some unknown reason, to appear." Best use of it is made in the postfever therapy and as a

general tonic. The technic of the subdural treatment is fully described, and primary atrophy is considered to be its indication par excellence as soon as fever therapy has demonstrated its inefficacy.

An entire new chapter is given to the intensive arsenotherapy of syphilis. It is shown that the incidence of hemorrhagic encephalitis is two hundred and twenty times greater with this type of treatment than with the other forms and that the fatalities from hemorrhagic encephalitis alone are at least four times the treatment fatalities from all other causes. The incidence of infectious relapse with the five day method is 12 per cent. Moore concludes that massive chemotherapy is a problem for the laboratory rather than for the clinic.

The beginner and the general practitioner will be attracted by the clear, didactic trend of the book; the syphilologist, by the attention given to all details, complications, therapeutic approaches, etc. The internist will find a comprehensive description of cardiovascular and visceral syphilis, and the neurologist will give his particularly careful attention to the chapters on neurosyphilis.

Shock Treatment in Psychiatry: A Manual. By Lucie Jessner, M.D., Ph.D., and V. Gerard Ryan, M.D. Pp. 149. New York: Grune & Stratton, Inc., 1941.

This is a concise and effective statement of the present status of shock treatment in psychiatry of whatever kind—insulin, metrazol, electric; the history, the method, the indications and contraindications, the complications, the physiologic changes involved, the actual results, statistical and individual, and their interpretation are all concisely and conservatively presented. There is an extensive bibliography, which includes many of the important contributions to this material.

It is gratifying to the reviewer to see two workers in this field, who obviously have had a great deal of experience, attempting to find out from individual cases the actual progress of therapeutic results. So much of past effort has been based on statistical treatment of results, and while this is absolutely necessary, of course, it is of little help in the evaluation of results in individual cases.

The reviewer can state from personal experience with prolonged coma that there is additional evidence that blood transfusion is an effective agent in terminating this unfortunate condition.

This book will be of considerable interest to practical workers in the psychiatric field and is heartily recommended to any student who wishes a quick and authoritative résumé of the whole situation of shock treatment.